COMPARITIVE STUDY OF INTRATHECAL ROPIVACAINE –FENTANYL AND BUPIVACAINE- FENTANYL FOR LOWER LIMB ORTHOPAEDIC SURGERIES

Dissertation Submitted

for the degree

DOCTOR OF MEDICINE BRANCH – X

(ANAESTHESIOLOGY) APRIL 2016

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI

CERTIFICATE BY THE HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled "**COMPARITIVE STUDY OF INTRATHECAL ROPIVACAINE –FENTANYL AND BUPIVACAINE-FENTANYL FOR LOWER LIMB ORTHOPAEDIC SURGERIES"** submitted by **Dr.R.Vijayendran**, in partial fulfillment for the award of the degree of Doctor of Medicine in Anaesthesiology by the Tamilnadu Dr.M.G.R. Medical University, Chennai , this is a bonafide original research work done by him in the department of Anaesthesiology and Critical Care, Tirunelveli Medical College, under my guidance and supervision during the academic year 2014-2016.

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DECLARATION BY THE CANDIDATE

I, **Dr.R.Vijayendran**, declare that the dissertation has entitled **"COMPARITIVE STUDY OF INTRATHECAL ROPIVACAINE –FENTANYL AND BUPIVACAINE- FENTANYL FOR LOWER LIMB ORTHOPAEDIC SURGERIES"** has been prepared by me. This is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai, in partial fulfilment of the requirement for the award of M.D. Degree, Branch X (ANAESTHESIOLOGY) degree examination to be held in April 2016.

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PROTOCOL TITLE: COMPARITIVE STUDY OF INTRATHECAL ROPIVACAINE - FENTANYL AND BUPIVACAINE FENTANYL FOR LOWER LIMB ORTHOPAEDIC SURGERIES.

PRINCIPAL INVESTIGATOR: Dr. R. VIJAYENDRAN, MBBS.,

DESIGNATION OF PRINCIPAL INVESTIGATOR: POST GRADUATE IN ANAESTHESIOLOGY
DEPARTMENT & INSTITUTION: TIRUNELVELI MEDICAL COLLEGE, TIRUNELVELI

Dear ,Dr. R. Vijayendran, MBBS., The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during the IEC meeting held on 10.06.2015.

THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1.	TIREC Application Form	☐
2.	Study Protocol	☐
3.	Department Research Committee Approval	☐
4.	Patient Information Document and Consent Form in English and Vernacular Language	☐
5.	Investigator's Brochure	☐
6.	Proposed Methods for Patient Accrual Proposed	☐
7.	Curriculum Vitae of the Principal Investigator	☐
8.	Insurance /Compensation Policy	☐
9.	Investigator's Agreement with Sponsor	☐
10.	Investigator's Undertaking	☐
11.	DCGI/DGFT approval	☐
12.	Clinical Trial Agreement (CTA)	☐
13.	Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA)	☐
14.	Clinical Trials Registry-India (CTRI) Registration	☐

THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
2. The date of commencement of study should be informed
3. A written request should be submitted 3weeks before for renewal / extension of the validity
4. An annual status report should be submitted.
5. The TIREC will monitor the study
6. At the time of PI's retirement/leaving the institute, the study responsibility should be transferred to a person cleared by HOD
7. The PI should report to TIREC within 7 days of the occurrence of the SAE. If the SAE is Death, the Bioethics Cell should receive the SAE reporting form within 24 hours of the occurrence.
8. In the events of any protocol amendments, TIREC must be informed and the amendments should be highlighted in clear terms as follows:
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   b. The PI must comment how proposed amendment will affect the ongoing trial. Alteration in the budgetary status, staff requirement should be clearly indicated and the revised budget form should be submitted.
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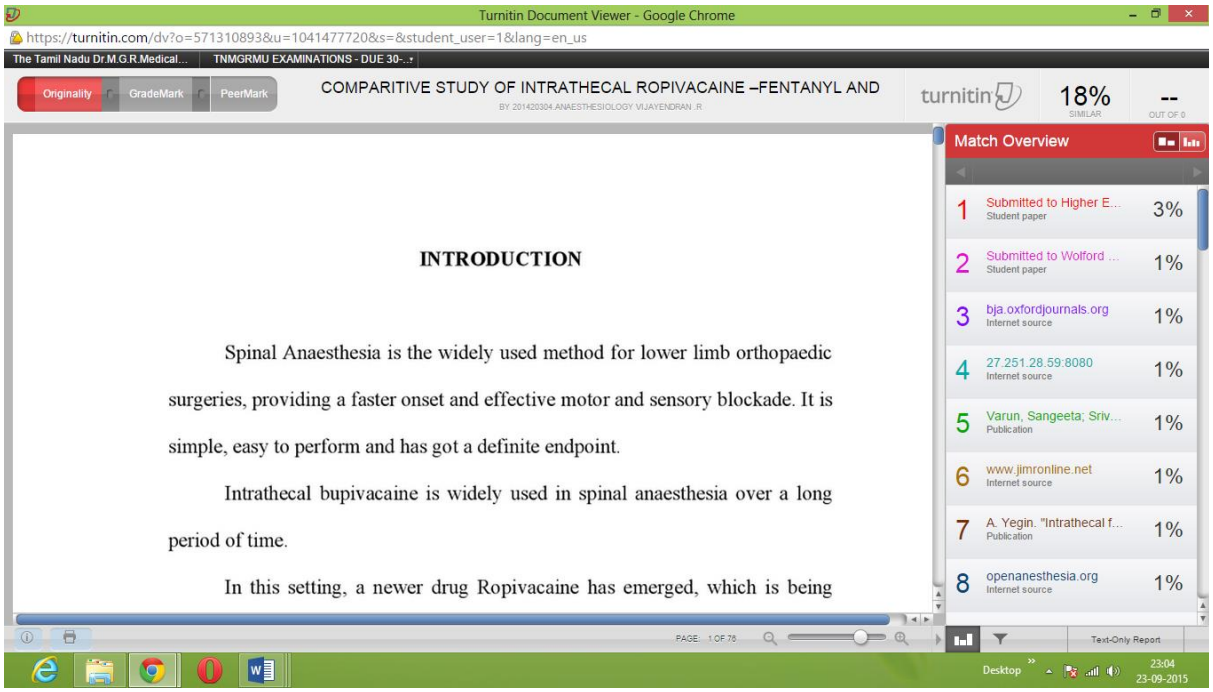
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INTRODUCTION
Spinal Anaesthesia is the widely used method for lower limb orthopaedic surgeries, providing a faster onset and effective motor and sensory blockade. It is simple, easy to perform and has got a definite endpoint.
Intrathecal bupivacaine is widely used in spinal anaesthesia over a long period of time.
In this setting, a newer drug Ropivacaine has emerged, which is being
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COMPARITIVE STUDY OF INTRATHECAL ROPIVACAINE –FENTANYL AND BUPIVACAINE- FENTANYL FOR LOWER LIMB ORTHOPAEDIC SURGERIES

Aim

Intrathecal bupivacaine results in a longer duration of complete anaesthetic block than ropivacaine. Fentanyl used as an adjuvant may improve the quality of spinal block of ropivacaine, while maintaining its advantage of early motor recovery.

The aim of the study was to compare the efficacy and safety of intrathecal ropivacaine-fentanyl (RF) with bupivacaine-fentanyl (BF) for lower limb orthopaedic surgeries.

Methods

In this Single Centered, Prospective, Randomized, Parallel group, Double – Blind study, sixty patients were randomly allocated to receive either intrathecal 15 mg of 0.5% ropivacaine with 25 mcg fentanyl (Group RF) or 15 mg of 0.5% bupivacaine with 25 mcg fentanyl (Group BF). The onset, duration, spread of sensory and motor block, haemodynamic parameters and side effects were recorded.

Data analysis was done by using SPSS software and Sigma Stat 3.5 version (2012).

Results

Time to reach highest sensory level, complete motor block and two segment sensory regression time were comparable. The motor recovery to Bromage scale 1 was faster in Group RF. The haemodynamic stability was better in Group RF. Time duration of analgesia was prolonged in Group BF .

Conclusion

Intrathecal RF provided satisfactory anaesthesia with Haemodynamic stability for lower limb orthopaedic surgeries. It provided a similar sensory but a shorter duration of motor block compared to BF, which is a desirable feature for early ambulation, voiding and physiotherapy.

Key words

Ropivacaine, bupivacaine, fentanyl, intrathecal, orthopaedic surgery.

INTRODUCTION

Spinal Anaesthesia is the widely used method for lower limb orthopaedic surgeries, providing a faster onset and effective motor and sensory blockade. It is simple, easy to perform and has got a definite endpoint.

Intrathecal bupivacaine is widely used in spinal anaesthesia over a long period of time.

In this setting, a newer drug Ropivacaine has emerged, which is being widely used for epidural blocks and nerve plexus blocks. Ropivacaine has an improved safety profile over bupivacaine with respect to central nervous system and cardio toxic potential. Though ropivacaine is being used frequently, in epidural and nerve blocks, the literature regarding its use in intrathecal route is sparse.

HISTORY OF SPINAL ANAESTHESIA

J.Leonard corning 1855 – 1923, A New York Neurologist, in 1885, while experimenting with cocaine on the spinal nerves, he accidentally pierced the dura of a dog. Later he deliberately repeated the intradural injection, called it spinal anesthesia and suggested it can be used in surgical procedures.

Heinrich Irchacus Quinke (1842 -1922) of Germany in 1891 and Essex wynter (1860 – 1945) in England, had standardized lumbar puncture in the same year.

In 1892 –the term 'conduction anaesthesia' was introduced by Heinrich Braun August Bier (1861 – 1949) in August 1898 in Kiel- Germany had performed the first planned spinal analgesia for surgery in man performed by injecting 3ml of 0.5% cocaine solution intrathecally into a 34 years old labourer.

In 1902, Heinrich Braun used Adrenaline to reduce toxicity and to increase the duration of spinal analgesia.

In 1957, Bupivacaine was synthesized by Ekenstam

In 1963, Bupivacaine was used clinically by LJ Telivuo

In 1979, Albright reported cardiac arrest following regional anesthesia using local anesthetics bupivacaine and etidocaine. He also reported presumed accidental intra vascular injection of either bupivacaine or etidocaine leading to sudden ventricular arrhythmias and also as severe convulsions.

This sequence of events provided the need to develop a newer local anesthetic drug with improved safety profile.

In 1996, Ropivacaine was introduced in clinical practice, and has consistently demonstrated an improved safety profiles over bupivacaine with a reduced CNS and cardio toxic profile.

Ropivacaine was approved for intrathecal administration by the European Union in February 2004.

ANATOMY& PHYSIOLOGY

The vertebral canal covering the human spinal cord extends from the foramen magnum to the sacral hiatus. The vertebral column forming the vertebral canal consists of

Cervical 7

Thoracic 12

Lumbar 5 vertebrae.

The sacrum 5 and

The coccyx 4 fused segments.

The adult spine has four curvatures-

Cervical and Lumbar - convex forwards (lordosis), which are formed by postural alignment.

Thoracic and Sacral -concave forwards (kyphosis).formed by the actual configuration of the vertebrae.

The vertebrae are held together by a number of overlapping ligaments namely

1. Anterior longitudinal ligament - On the anterior surface of the

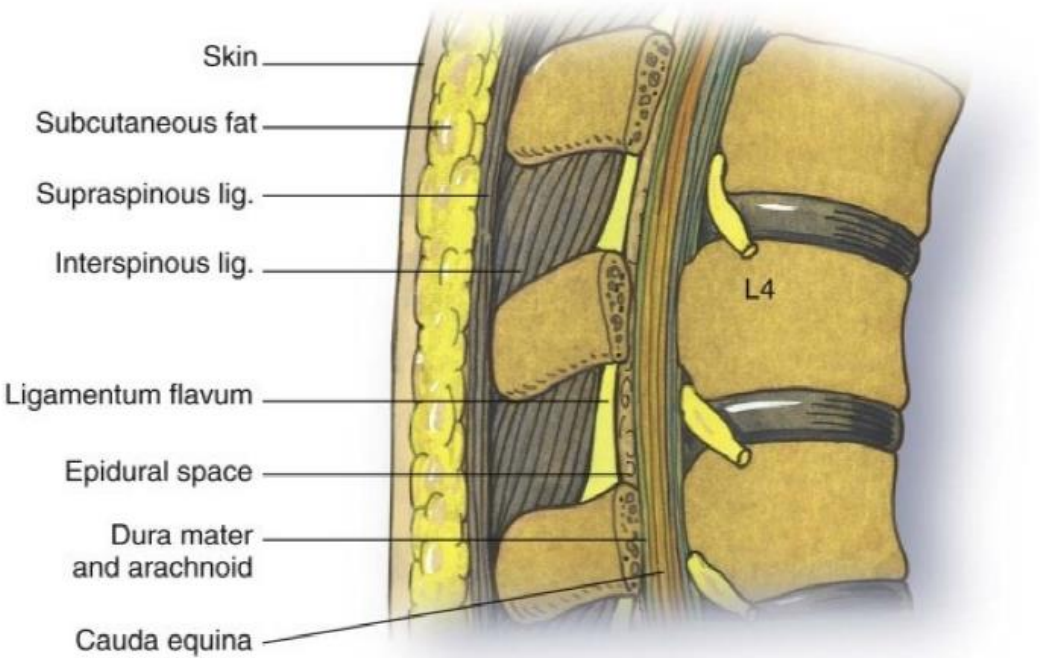
Vertebral body

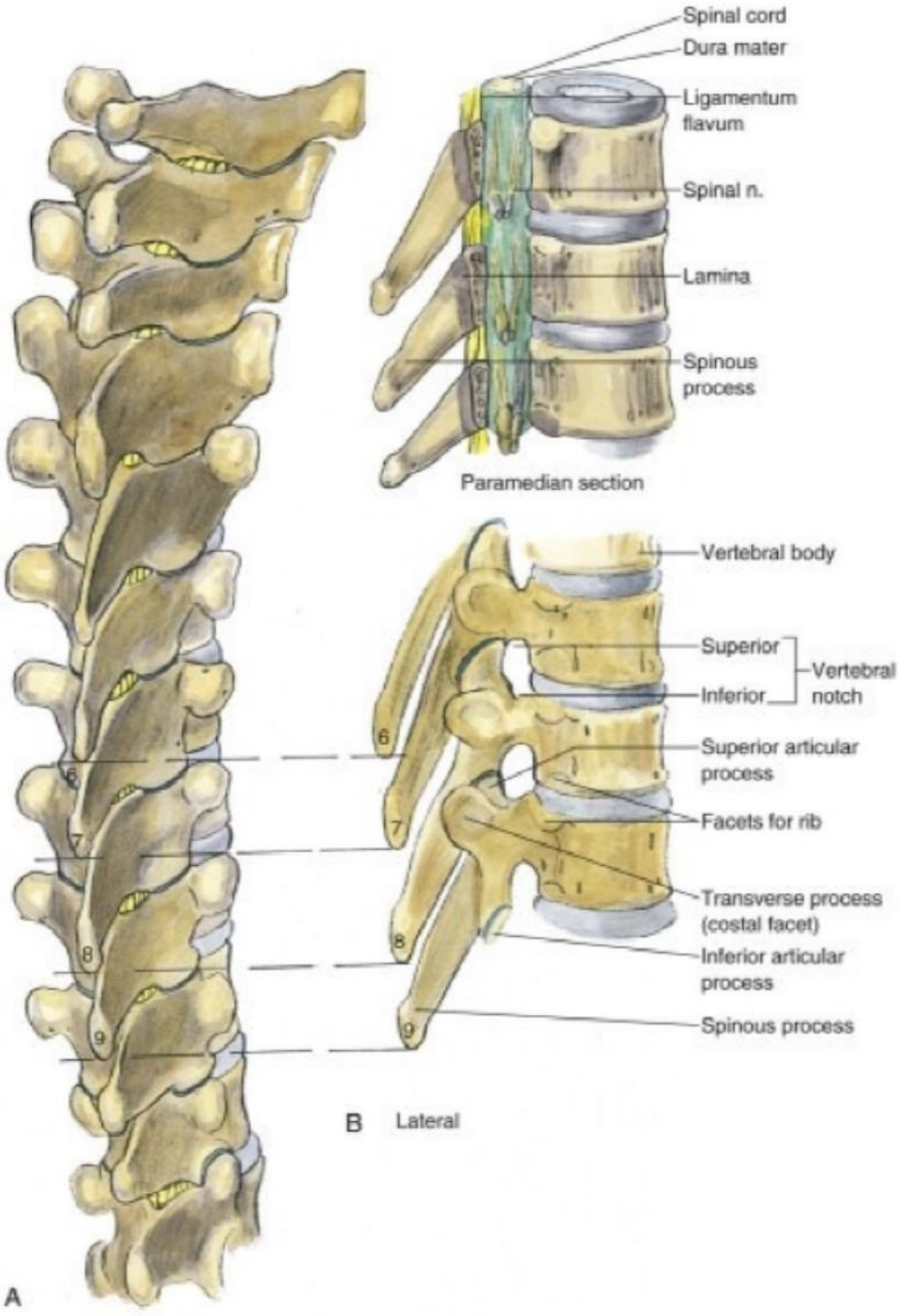
2. Posterior longitudinal ligament - On the posterior surface of

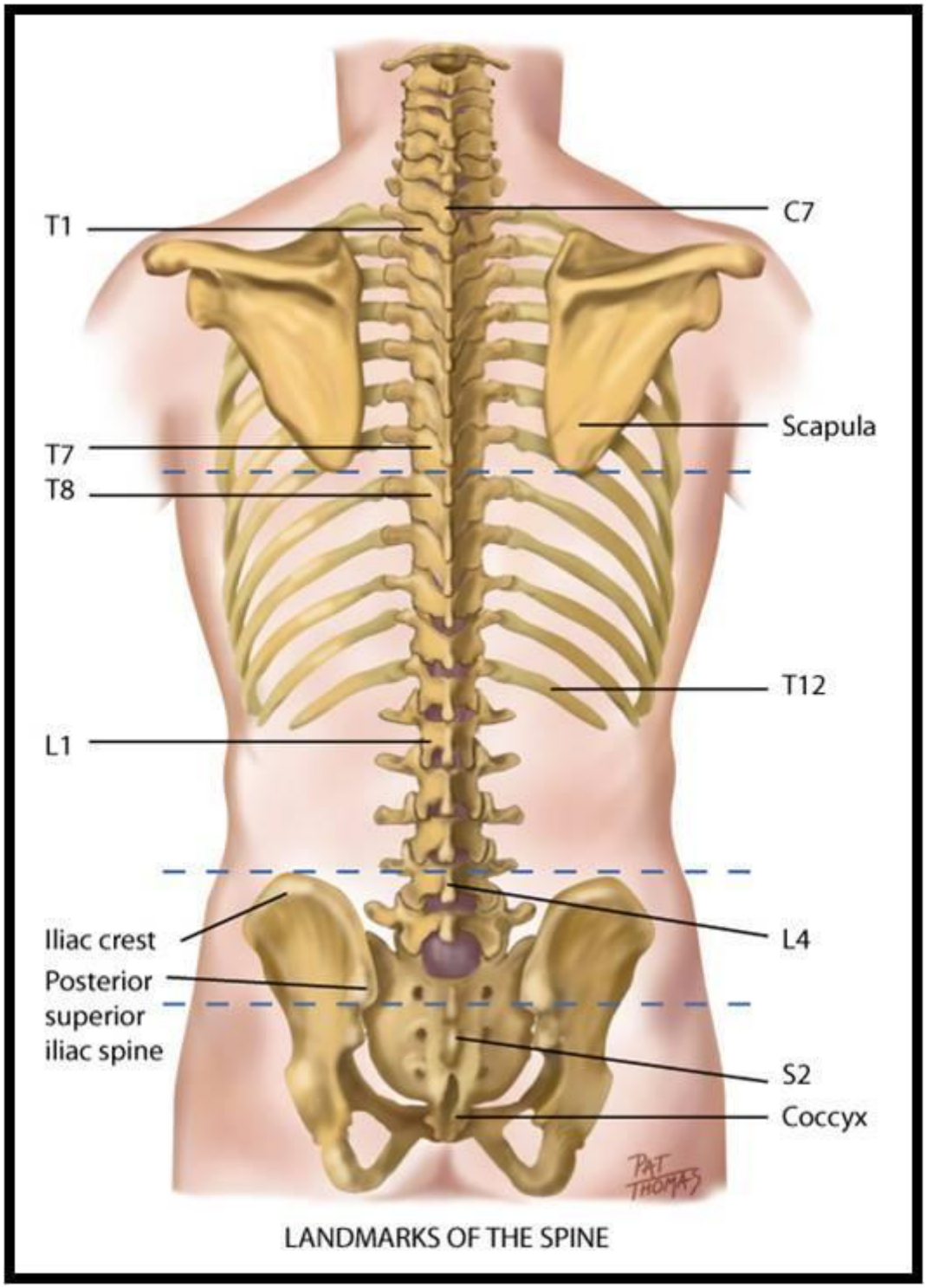
   Vertebral body.

3. The Ligamentum flavum- Running from lamina to lamina composed of yellow elastic fibers and it is thicker from above downwards.

4. Supraspinous ligament
5. Inter spinous ligament and
6. Intervertebral discs.




Spinal cord
Dura mater
Ligamentum flavum
Spinal n.
Lamina
Spinous process
Paramedian section
Vertebral body
Superior
Inferior
Vertebral notch
Superior articular process
Facets for rib
Transverse process (costal facet)
Inferior articular process
Spinous process
6
7
8
9
B Lateral
A
Oblique
Ligamenta flava



LANDMARKS OF THE SPINE

Certain common palpable landmarks that usually correspond to a particular level include

1. The seventh cervical vertebra - the most prominent spinous process
2. The seventh thoracic vertebra -inferior angle of scapula
3. Tuffier's line, the line connecting the two iliac crests almost

Crosses the vertebral column at the level of L4-L5 intervertebral space.

The intervertebral canal consists of:

1. Roots of spinal nerves
2. Spinal membrane with the spinal cord and cerebrospinal Fluid.
3. Vessels, fat and areolar tissue.

The spinal cord is the continuation of medulla oblongata and it ends below in conus medullaris from which filum terminale, descends vertically as cauda eqina. From the upper border of atlas, the Spinal cord extends upto the lower border of first lumbar vertebra in adults. The spinal cord extends till the upper border of the second lumbar vertebra, and still lower in infants.

The coverings of spinal cord from inside to outside are

- Piamater.
- Arachnoidmater
- Duramater.

The Duramater is attached to the margins of the foramen magnum above and ends at the level of lower border of second sacral vertebra below. From the Spinal Cord, the posterior and anterior nerve roots pierce the investing layer of

duramater, and carries the prolongation (dural cuff). The dural cuff then blends with the perineurium of mixed spinal nerve.

The Arachnoid mater is a thin transparent sheath which is closely applied to the duramater. The subdural space is a potential space which allows the dura and arachnoid to move over each other. It contains a small amount of serous fluid.

The spinal cord is invested closely by the Piamater. From each lateral surface of the piamater, the denticulate ligament projects into the subarachnoid space. The piamater inferiorly ends as a prolongation, which is termed as the filum terminale, gets attached to the periosteum of coccyx after penetrating the distal end of the dural sac.

The subarachnoid space is filled with the cerebrospinal fluid and it contains the denticulate ligament and the spinal nerve roots. Lumbar puncture is routinely done below the second lumbar vertebra to L5-S1 interspace in order to avoid damage to the spinal cord, which ends at the lower border of first lumbar vertebra.

Blood supply of spinal cord

The spinal cord receives its blood supply mainly from three Longitudinal arterial channels namely

- One anterior spinal artery, arising by the union of a small branch from each vertebral artery and it supplies the lateral and the anterior columns.

- Two posterior spinal arteries, branches of posterior inferior cerebellar arteries on each side, with no anastomosis between them, supply the posterior columns of the cord.

The spinal arteries also receive blood through radicular arteries that reaches the cord along the roots of spinal nerves. These radicular arteries arise from the vertebral, ascending cervical, deep cervical, the intercostals, lumbar and sacral arteries. The arteria radicularis magna, also called as Artery of Adamkiewicz, is the largest of the radicular arteries and it may be responsible for supplying blood to the lower two-thirds of the spinal cord. It is variable in position. There is no anastomosis between the anterior spinal artery and the posterior spinal artery. So if thrombosis occurs in any of these arteries, spinal cord infarction will occur.

The Venous drainage of the spinal cord is mainly through six longitudinal venous channels. They are;

1. Anteromedian and
2. Postero median venous channels
3. Two pairs of Anterolateral and Posterolateral channels.

These channels join together forming a venous plexus, from where the venous blood drains through the radicular vein into the vertebral veins in the neck, the azygos veins in the thorax, the lumbar veins in the abdomen and the lateral sacral veins in the pelvis.

CEREBROSPINAL FLUID

The cerebrospinal fluid is an Ultra filtrate of plasma secreted by the choroid plexus of the third, fourth and lateral ventricles at a rate of 0.3 to 0.5ml/min.

The average volume of CSF ranges from 120 to 150 ml, of which 25 ml is in the cerebral subarachnoid space, 35 ml in the ventricles and about 75 ml is in the spinal subarachnoid space. It is a colourless liquid with slight opalescence due to the presence of globulin.

Circulation of cerebrospinal fluid

The CSF is produced as an Ultra filtrate by the choroid plexuses of the lateral ventricles, passes through the interventricular foramina (of Monro) into the third ventricle, and then through the cerebral aqueduct (of Sylvius) into the fourth ventricle. CSF flows through foramen of Magendie and foramen of Luschka to reach the spinal subarachnoid space. The amount of CSF in spinal canal is 75 ml with a pressure of 70-180 mm of H_2O in lateral position and about 375-500mm of H_2O in vertical position.

The cerebrospinal fluid is absorbed mainly into the venous system, through the arachnoid villi and the arachnoid granulations. These are most numerous in superior sagittal sinus and its lateral lacunae. Approximately 300-380 ml of cerebrospinal fluid enters venous circulation each day.

An important factor determining the spread of drug in CSF is the specific gravity of the drug , in relation to that of CSF, which is 1.003 – 1.009 (average1.004). Hyperbaric solution is one which is denser than CSF at 37^0 C.

The Specific gravity of 10% Dextrose, used commonly in the so called heavy or hyperbaric solutions is 1.034.

Physical Characteristics of Cerebrospinal Fluid

pH: 7.4

Specific gravity at body temperature: 1.007

Specific gravity at 4 degree Celsius: 1.0003

Density: 1.0003gm/ml

Baricity: 1.000

Cells: 3 – 5 / cu.mm

Proteins: 20mg / dl

Glucose: 45 – 80 mg/dl

THE SPINAL CORD

The Spinal Cord is a part of the nervous system, which occupies the upper 2/3 of the vertebral canal, and is usually 45cm long. It extends from upper border of the atlas to the upper border of the second lumbar vertebra, and lower still in infants. It is continuous as medulla oblongata upwards and ends below in conus medullaris. The nerve roots which pass out in transverse direction in early life becomes more oblique in direction in adults. They are bathed in CSF and will be readily affected by the local analgesic solution injected in the lumbar area.

SEGMENTS OF SPINAL CORD:

The spinal cord is divided into many segments by the pairs of spinal nerves, which arise from it. These pairs are 31 in number.

a) Cervical 8

b) Thoracic 12

c) Lumbar 5

d) Sacral 5 and

e) Coccygeal 1

The nerve roots within the duramater have no epineural sheaths, so they are easily affected by the local analgesics. The cord is not transversely blocked by spinal analgesia.

Spinal nerves;

Anterior root is efferent and motor. The Posterior root is larger than anterior and is largely sensory. Posterior root has a ganglion and it conveys fibers of all sensation with automatic fibers.

Pain pathway in the spinal cord:

Pain and temperature fibers enter the posterior horn, where they end around cells in the grey matter. These fibers then cross to the contra lateral side within two to three segments, and then ascend to the thalamus via the lateral spino thalamic tract. Tactile impulses ascend through the ventral spinothalamic tract to the thalamus. The deep pressure and muscle sensory impulses ascend through the posterior columns and the spinocerebellar tracts. The Vibration sense impulses ascend in the posterior columns.

The Anterior and posterior nerve roots within its sheath unite in the intervertebral foramen to form the main trunk, which soon divide into anterior and posterior divisions.

Local analgesic drugs injected into the sub arachnoid space can traverse along the nerve trunk for as much as 2cm beyond the inter vertebral foramen. The Analgesic drugs affect autonomic, sensory and motor fibers in that order and fibers which gets blocked easily will hold the drug longest, and thus sensory block lasts longer than motor, and usually ascends two segments higher up the cord than motor block.

Segmental levels:

Clavicle	C3 – C4
Second inter costal space	T2
Nipple line	T4 – T5
Sub costal arch	T6 – T8
Umbilicus	T10
Inguinal region	L1
Perineum	S1 – S4

Segmental levels of spinal reflexes:

Epigastric	T7 T8
Abdominal	T9 - T12
Cremasteric	L1 L2
Plantar	S1 S2

MECHANISM OF ACTION OF LOCAL ANESTHETIC DRUGS

The Local anesthetic solution which is injected into the subarachnoid space gets mixed with the cerebrospinal fluid, and comes into contact with the spinal cord and the peripheral nerve roots. The nerve roots leaving the spinal canal gets exposed readily to the local anesthetic solution, since they are not covered with epithelium. Local anesthetic drugs prevent the nerve impulse transmission (conduction blockade) by inhibiting the passage of sodium ions, through the ion-selective sodium channels in nerve membranes. The failure of the sodium ion channel permeability to increase, in turn leads to slowing down of the rate of depolarization, so that a threshold potential is not reached, and so an action potential is not propagated. These local anesthetic drugs do not alter the resting membrane potential or the threshold potential.

Zone of Differential Blockade

In subarachnoid block, sympathetic fibers are blocked about two to six segments higher than the sensory fibers. When more concentrated solutions are used or when adrenaline is added, sympathetic block will be greater. Motor block will be two segments below the level of sensory block.

Nerve fibers are blocked in the following order;

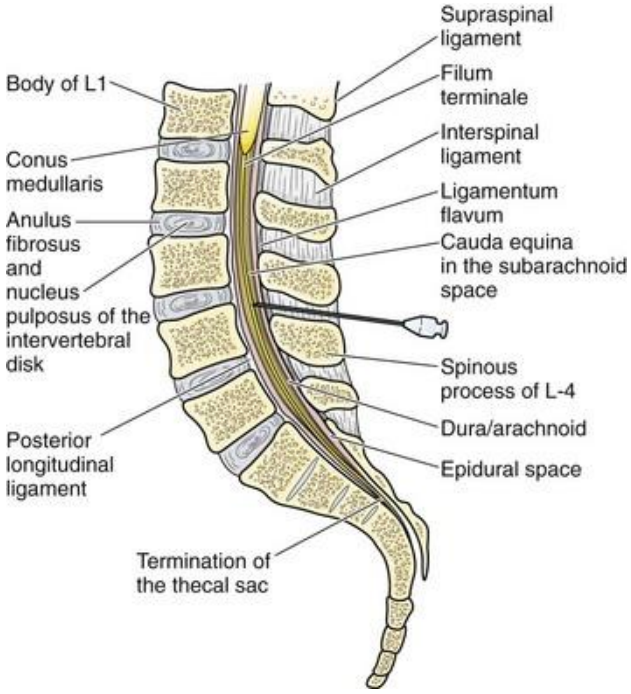
1. Autonomic preganglionic B fibers,
2. Temperature fibers- Cold fibers first, then followed by warm fibers
3. Pinprick fibers
4. Fibers conveying pain, greater than pin prick
5. Touch fibers

6. Deep pressure fibers

7. Somatic motor fibers

8. Fibers conveying vibratory sense and proprioceptive impulses.

During recovery, the sensations return in the reverse order, but it has been suggested that the sympathetic activity returns before sensation.



Subarachnoid block

SPREAD OF LOCAL ANAESTHETICS IN SUBARACHNOID SPACE

The local anesthetic drug is diluted by CSF and therefore its original concentration is less than the actual mass of drug injected. Spread is also determined by the baricity of the injected solution. Baricity is a ratio of comparing the densities of a local anesthetic solution at a specific temperature, with the density of CSF at the same temperature. A hypobaric solution has a baricity of less than 1.0000 or specific gravity less than 1.0069 (the mean value of specific gravity). A hyperbaric solution has a baricity of greater than 1.0000 or specific gravity more than 1.0069. Hypobaric and Hyperbaric solutions are prepared from isobaric solutions by the addition of various amounts of sterile distilled water and dextrose respectively. Isobaric solutions do not move under the influence of gravity in the CSF. Hyperbaric solutions, being heavier than CSF, settle to the most dependent aspect of the subarachnoid space, which is determined by the position of the patient. In supine patient, hyperbaric solutions gravitate to the thoracic kyphosis. Hypobaric solution floats up against the gravity to the nerves innervating the corresponding area supplying the surgical site.

FATE OF LOCAL ANAESTHETICS IN SUBARACHNOID SPACE

After injection of local anesthetic solution into subarachnoid space, its concentration falls rapidly. The initial steep fall is due to the mixing of local anesthetic with CSF and subsequent absorption into nerve roots and spinal cord. The removal of local anesthetic solution following subarachnoid injection is primarily by the mechanism of vascular absorption. Depending on the type of the drug used, it is metabolized in plasma by pseudo cholinesterase or in the liver. The addition of a vasoconstrictor to the local anesthetic solution will increase the duration of anaesthesia by decreasing the absorption of the drug.

PHYSIOLOGICAL EFFECTS OF SUBARACHNOID BLOCK

Cardiovascular effects

The vasomotor tone is determined by the sympathetic fibers which are arising fromT5 to L1 and innervating the arterial and venous smooth muscles. Hence sympathetic block will cause a decrease in the blood pressure, which may be accompanied by bradycardia. With high sympathetic blockade, sympathetic cardiac accelerator fibers arising at T1-T4 are blocked, leading to a decreased cardiac contractility. Bezod -Jarisch reflex has been known as a cause of hypotension, bradycardia, and cardiovascular collapse after central neuraxial blockade, and in particular, subarachnoid block.

Respiratory effects

Even with high thoracic levels, the tidal volume remains unchanged. A small decrease in the vital capacity is due to paralysis of abdominal muscles which are necessary for forced exhalation, and not due to phrenic nerve involvement or impaired diaphragmatic function. Effective coughing and clearing of secretions may get affected with higher levels of block. Respiratory arrest associated with spinal anaesthesia is rare and is due to hypo perfusion of respiratory centers in the brain stem.

Gastrointestinal function

Nausea and vomiting is seen in up to 20% of patients. It is due to gastro intestinal hyperperistalsis caused by unopposed parasympathetic activity. Vagal tone dominance results in a small and contracted gut with active peristalsis and

can provide excellent operative conditions. The Hepatic blood flow will decrease with reductions in mean arterial pressure.

Renal function

Renal function has a wide physiological reserve. Any decrease in the renal blood flow is of little physiological importance. Neuraxial blocks frequently causes urinary retention, which delays the discharge of out patients and necessitates urinary bladder catheterization of inpatients.

INDICATIONS FOR SUBARACHNOID BLOCK

Spinal anaesthesia can be administered usually for surgeries such as

- Lower abdominal surgeries
- Lower limb surgeries
- Urological procedures
- Obstetric procedures
- Gynecological surgeries
- Perineal and rectal surgeries

CONTRAINDICATIONS FOR SUBARACHNOID BLOCK

The absolute contraindication for subarachnoid block are

- Patient refusal
- Local sepsis

The relative contraindications include

- Raised intracranial pressure
- Coagulopathy
- Neurological disease
- Fixed cardiac output states
- Any documented allergy to local anesthetics
- Major spine deformities or previous surgery on the spine
- Hemodynamic instability.

FACTORS INFLUENCING HEIGHT OF ANALGESIA IN SUB ARACHNOID BLOCK

- Dose of the drug injected
- Volume of fluid injected
- Specific gravity of the anesthetic drug solution
- Position of the patient during injection
- Posture of the patient after injection
- Choice of interspace
- Patient factors- Age, Height and Pregnancy

FACTORS NOT INFLUENCING HEIGHT OF ANALGESIA IN SUBARACHNOID BLOCK

- Patient factors- Weight, Sex.
- Barbotage.
- Rate of speed of injection.
- Composition and circulation of cerebrospinal fluid.
- Direction of bevel of the standard needle (although not of the Whitacare needle).

COMPLICATIONS OF SUBARACHNOID BLOCK

The Immediate complications include

- Hypotension
- Bradycardia
- Toxicity due to intravascular injection
- Allergic reaction to local Anesthetic
- Hypoventilation (brain stem hypoxia)

The late complications include

- Post-dural puncture headache
- Retention of urine
- Backache
- Meningitis
- Transient neurological symptoms
- Cauda equine syndrome
- Anterior spinal artery syndrome
- Horner’s syndrome

LOCAL ANAESTHETIC DRUGS

Local anesthetic agents are divided into two groups namely the Amides and esters

Esters

1.Benzocaine

2.Chloroprocaine

3.Cocaine

4.Cyclomethycaine

5.Dimethocaine

6.Piperocaine

7. Propoxycaine

8.Procaine

9.Proparacaine

10.Tetracaine/Amethocaine

Amides

1. Articaine

2. Bupivacaine

3. Dibucaine

4. Etidocaine

5. Levobupivacaine

6. Lignocaine

7.Mepivacaine

8. Prilocaine

9. Ropivacaine

10. Trimecaine

Adjuvants used in spinal anesthesia

Adjuvants are intended to prolong the local anesthetic analgesia and reduce their toxic doses. Some of the adjuvants used intrathecally are

Opioids-

Morphine, Diamorphine, Fentanyl, Sufentanyl

Clonidine

Ketamine

Neostigmine

Adrenaline

Phenylepherine

Sodium bicarbonate

BUPIVACAINE

Bupivacaine, an amino amide local anesthetic. It was first synthesized in Sweden by A.F Ekenstam and his colleagues in 1957.First report of its use was in 1963 by L.J Teluvio. It is one of the long acting local anesthetic agents available,which is extensively used for intrathecal, extradural and peripheral nerve blocks. It is a white crystalline powder soluble in water.

CHEMICAL STRUCTURE OF BUPIVACAINE

1-butyl-n-(2, 6 –dimethylphenyl) piperidine-2-carboxamide

Physiochemical properties

- Molecular formula; C18 H28 N2OHCl
- Molecular weight; 288.43 g/mol
- Solubility in water 25mg/ml
- pH of saturated solution 5.2
- pKa 8.1
- Specific gravity 1.021 at 37 ◦ C
- Melting point 247 – 258 ◦ C

Mechanism of action:

Mechanism of action of bupivacaine is similar to that of any other local anaesthetic .The primary action of local anaesthetics is on the cell membrane axon, on which it produces electrical stabilization. Bupivacaine prevents the nerve impulse transmission (conduction blockade) by the inhibition of the

sodium ion passage through the ion-selective sodium channels in the nerve membranes. The sodium channel is a specific receptor for the local anaesthetic molecules. Failure of the sodium ion channel permeability leads to slowing down of the rate of depolarization, so that the threshold potential is not reached, and thus an action potential is not propagated. Local anaesthetics do not alter the resting transmembrane potential or the threshold potential. The mechanism by which local anaesthetics block sodium conductance is as follows:

1. Local anaesthetics in the cationic form act on the receptors within the sodium channels on cell membrane and block it. The local anaesthetics can reach the sodium channel either via the lipophilic pathway directly across the lipid membrane, or via the axoplasmic opening. This mechanism accounts for 90% of the nerve blocking effects of amide local anaesthetics.

2. The second mechanism of action is by membrane expansion. This is a non specific drug receptor interaction.

Other site of action targets:

- Voltage dependent potassium ion channels
- Calcium ion currents (L-type most sensitive)
- G protein coupled receptors

Dosage depends on:

- Area to be anaesthetized
- Number of nerve segments to be blocked
- Individual tolerance to the drug
- Technique of administration of local anaesthesia.
- Vascularity of area

Bupivacaine is available in the following concentrations:

- 0.25%. 0.5%and 1%
- 0.25% and 0.5% solution in isotonic saline
- 0.5% solution in 8% dextrose

Dosage is 2mg/kg limited to 150 mg in four hours. The intrathecal minimum local analgesic dose of Bupivacaine is 2.37 mg**.**

Type of block	**Concentration %**	**Dosage in ml**	**Dosage in mg**
Local infiltration	0.25 – 0.5	5 – 20	Up to 175 mg
Intercostal nerve block	0.25 – 0.5	3 – 5 /nerve	15 – 20/nerve
Brachial plexus Block	0.25 – 0.5	15 – 30	75 – 225
Caudal block	0.25 – 0.5	15 - 30	75 – 150
Epidural block	0.25 – 0.5	15 – 30	50 - 200
Sub arachnoid block	0.5 – 0.75	02-04	10-20

These doses may be repeated in 3 -4 hrs, but the maximum dose in 24 hrs is 400 mg. Addition of vasoconstrictor produces a very slight increase in the duration of action. However the peak blood level of bupivacaine is significantly reduced, thereby minimizing the systemic toxicity.

ANESTHETIC POTENCY:

Hydrophobicity appears to be a primary determinant of the intrinsic anesthetic potency, and Bupivacaine is highly hydrophobic, hence it is very potent.

ONSET OF ACTION:

The onset of conduction blockade depends on the dose of the local anesthetic used. The onset of action of Bupivacaine is between 4– 6 mins and maximum anaesthesia is obtained in 15 – 20 minutes.

DURATION OF BLOCK:

The duration of anesthesia varies according to the type of block, the average duration of peridural block is about 3.5 – 5 hours, it is about 5 – 6 hours for nerve blocks.

PHARMACOKINETICS:

The concentration of Bupivacaine in blood is determined by the amount injected, the rate of absorption from the site of injection, the rate of tissue distribution, vascularity and the rate of biotransformation and excretion of Bupivacaine. Bupivacaine can be detected in the blood within 5 mins of infiltration or following epidural or intercostals nerve blocks. Plasma levels are related to the total dose administered.

Peak levels of 0.14 to1.18 μg/ml were found within 5 mins to 2 hrs, and they will gradually decline to 0.1 to 0.34 μg/ml by 4 hrs.

PLASMA BINDING:

In plasma, drug binds avidly with protein to the extent of 70 -90%.

ABSORPTION:

The site of injection of drug used, dose and the addition of a vasoconstrictor determine the systemic absorption of Bupivacaine. The maximum level of Bupivacaine in the blood is related to the total dose of the drug administered from any particular site. Absorption is faster in areas of high vascular supply.

TOXICITY

The toxic plasma concentration is set at 4 – 5 μg/ml. Maximum plasma concentration rarely approach toxic levels. Ventricular arrhythmias, and ventricular fibrillation may occur more often after rapid administration of large doses of bupivacaine intra venously.

The pregnant patient is more sensitive to cardiotoxic effects of bupivacaine. 0.75% bupivacaine is no longer recommended for its use in obstetric anaesthesia.

There is no established role of antiarrhythmic drugs or traditional drugs in the setting of bupivacaine induced cardiac arrest. The first treatment for accidental intra vascular injection of overdose of anaesthetic are

- Securing the airway
- Oxygenation, ventilation

DISTRIBUTION:

The two-compartment model can describe this. The rapid distribution phase is mainly due to the uptake by rapidly equilibrating tissues. i.e.,the tissues having high vascularity. The slow distribution phase is mainly a function of distribution to slowly equilibrating tissues, biotransformation of the drug and excretion of the compound. More highly perfused organs show higher concentrations of the drug. Bupivacaine is rapidly excreted by the lung tissue. Though skeletal muscles does not show any particular affinity for bupivacaine, they are the largest reservoir of the drug.

DISTRIBUTION CHARACTERISTICS:

T1/2: 2-7 minutes (uptake by rapid equilibrium tissue)

T1/2: 28 minutes (distribution by slowly perfused tissues)

T1/2: 3-5 hours (metabolism and elimination)

VDSS: 72 liters (volume of distribution at steady state)

Pharmacodynamics:

Central Nervous System:

Bupivacaine readily crosses the blood brain barrier, causing CNS depression following higher doses. The initial symptoms of CNS toxicity involve feeling of dizziness, and light-headedness followed by auditory and visual disturbances. Drowsiness and disorientation may occur. Objective signs, are usually excitatory in nature, which includes muscular twitches, tremors and shivering, characterized by involvement of muscles of the face (perioral numbness) and part of the extremities. At still higher doses, cardiovascular or respiratory arrest may occur. Acidosis will increase the risk of CNS toxicity from Bupivacaine, since an elevation of the PaCO2 enhances the cerebral blood flow, which leads to more of anesthetic being delivered rapidly to the brain.

Autonomic nervous system:

Bupivacaine does not inhibit the Noradrenaline uptake and hence has no sympathetic potentiating effect. Myelinated preganglionic B fibers have a faster conduction time, and they are more sensitive to the action of Bupivacaine. When

used for conduction blockade, all local anesthetics, in particular-bupivacaine produces higher incidence of sensory than motor fibers.

Cardiovascular System

The primary cardiac electrophysiological effect of a local anesthetic is a decrease in the maximum rate of depolarization in Purkinje fibers and ventricular muscle. This action by Bupivacaine is far greater when compared to Lignocaine. Also, the rate of recovery of block is slower with Bupivacaine. Therefore there is complete restoration of Vmax between action potential particularly at higher rates. Therefore Bupivacaine is highly arrythmogenic. Bupivacaine reduces the cardiac contractility by blocking the calcium transport. Low concentration of Bupivacaine produces vasoconstriction whereas high doses cause vasodilatation.

Respiratory System:

Respiratory depression may be caused if an excessive plasma level is reached, and will result in the depression of medullary receptor center. The depression of respiration may be also caused by paralysis of the respiratory muscles of diaphragm, as may occur in high spinal or total spinal anesthesia.

Biotransformation and Excretion:

Bupivacaine undergoes the process of enzymatic degradation primarily in the liver. The excretion occurs primarily via the kidney. Urinary excretion is affected by renal perfusion and factors that affect the urinary pH. Less than 5% of bupivacaine is excreted through the kidney unchanged through urine. The major portion of injected drug appears in urine in the form of 2, 6 pipecolyoxylidine (ppx), which is a n-dealkylated metabolite. The renal

clearance of the drug is inversely related to its capacity of protein binding and pH of urine.

Adverse Effects:

Adverse effects are encountered in clinical practice mostly due

To overdose, inadvertent injection intravascularly, or slow metabolic degradation.

CNS:

It is characterized by excitation, or depression. The first symptom may be nervousness, dizziness, blurring of vision or tremors, which is followed by drowsiness, convulsions, unconsciousness and finally respiratory arrest.

CVS:

Myocardial depression, hypotension, arrhythmia, ventricular type conduction defect, SA node depression and cardiac arrest.

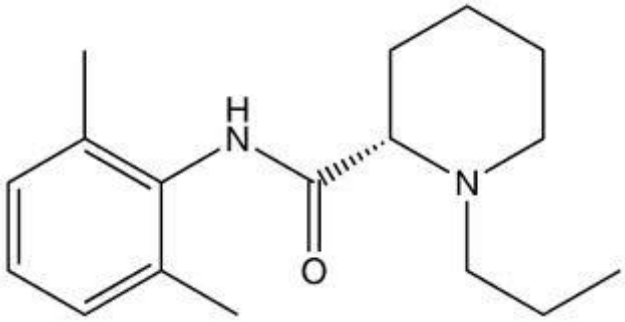
ALLERGIC REACTIONS:

Utricaria, bronchospasm, hypotension.

OTHERS:

Nausea, vomiting, chills, constriction of pupil and tinnitus.

ROPIVACAINE



History

Long acting local anaesthetic bupivacaine was released in 1965. Although bupivacaine has been the local anaesthetic of choice for decades with long duration of action, when given accidentally as intravascular, it produces irreversible cardio vascular collapse. Cardio toxicity with bupivacaine often proves difficult (or) impossible to treat. Prolonged motor block is another drawback of Bupivacaine. Because of these problems newer agents were looked into and Ropivacaine was released in 1996 and only recently launched in India.

Pharmacology

It is an amide group of local anaesthetic drug. It comes in the group of mepivacaine and bupivacaine. Instead of methyl group in mepivacaine, ropivacaine has a propyl group and bupivacaine has a butyl group. Mepivacaine and bupivacaine are currently used clinically as a racemic mixture of enantiomers containing equal properties of ‘R’ and ‘S’ forms. Ropivacaine is prepared from the alkylation of S-enantiomer of dibenzoil-L-tartaric acid.

The Pure-S-enantiomer is available as a preservative free clear solution in ampoules or vials in concentration of 0.2%, 0.5% and 0.75%. The solution has pH of 4.6 with a pKa 8.1. It binds extensively with plasma proteins (mainly one & acid glycoprotein) metabolized mainly in the liver and excreted by the kidneys. It readily crosses the placenta. The Pharmacodynamic parameters are similar to other amide agents. Like other local anaesthetic drugs ropivacaine works by reversible inhibition of Na^+ ion influx in nerve fibers and thereby temporarily stopping electrical conduction.

It is 10 times less lipid soluble when compared to bupivacaine and hence they are less likely to penetrate the larger myelinated motor fibers. It has a more selective action on A and C fibers as compared to A fibers. It has a less depression of cardiac conductivity and QRS interval. It is available only as isobaric solution.

Isobaric verses Hyperbaric Solution:

Density of a solution is the weight in gms of 1ml of that solution at 37^0C.

Specific gravity is the ratio of the density of the solution with the density of the water.

Baricity is defined as the ratio obtained by comparing the density of one solution to another.

To make a drug hypobaric to CSF, it must be less dense than CSF i.e.1, 0000

By adding water and warming the drug to 37^0C from 4^0C, it becomes hypobaric.

Dose:

Upto 3mg per kg.

Based on patient.

Route of administration and type of surgery.

Contraindication:

Allergy to amide LA

Bier's block – i.v regional anesthesia.

Uses:

Epidural / caudal block

Intra thecal block

Nerve block

Local infiltration

Local instillation

To establish a surgical anaesthesia through an epidural 10 – 20mls of 0.5% to 0.75% Ropivacaine is used depending on patient size and height of the block required. For postop and labour pain relief using an epidural 10mls/hr of 0.2%. Ropivacaine with fentanyl 2-4mg/ml can be used.

When used in epidural infusions 0.2% Ropivacaine is used for nerve blocks is fast with the motor block wearing off much earlier than compared to Bupivacaine.

It is available as only isobaric solution. Spinal Ropivacaine (0.75%) 2.5 – 4 mls with additives like Fentanyl and clonidine offers a reliable cardio stable

anaesthesia of the lower abdomen and limbs. Speed of onset is slower when compared to Bupivacaine.

For the same volume intrathecal, the height of the block with isobaric Ropivacaine 0.75% is significantly lower as compared to hyperbaric Bupivacaine (0.5%) Addition of clonidine, Dexmedetomidine prolongs analgesia upto 16hrs (Beware Bradycardia).

The Safety of Ropivacaine has been studied extensively. In a classic canine study (aroban in 2001), open chested dogs were randomized to escalating infusions of Bupivacaine, Ropivacaine and Levobupivacaine to permit collapse of the cardiovascular system.

Unsuccessful resuscitation from Ropivacaine, levobupivacaine and Bupivacaine was 10%, 30% and 50%. Larger doses and blood concentrations of Ropivacaine was well tolerated when compared to Levobupivacaine and Bupivacaine. Several studies and case reports have also established the safety of the Ropivacaine.

Cardiotoxicity of local anesthetics may be compared by the use of CC/CNS dose ratio. It is defined as the ratio of the dose causing cardiac collapse (CC) to the dose causing convulsions. The lower the number, the more cardiotoxic is the drug (ex. The CC/CNS for bupivacaine is approximately 3 versus 5 for ropivacaine).

REVIEW OF LITERATURE

Gaurav Kuthiala and Geeta Chaudhary [1] reviewed the pharmacological use of ropivacaine. They described that ropivacaine causes a reversible sodium ion influx inhibition, thereby it blocks the conduction of impulse in nerve fibers. This action of ropivacaine is potentiated by the inhibition of the potassium channels in a dose-dependent manner. The lipophilicity of ropivacaine is less when compared to bupivacaine, and so is less likely to penetrate the large myelinated motor fibers; and so, it has selective action on A δ and C nerves which were transmitting pain, comparing to Aβ fibers, which are involved in the motor function.

Luck et al [2] used equal doses of hyperbaric bupivacaine, ropivacaine and levobupivacaine (15 mg) intrathecally for elective surgery, and found that ropivacaine provided spinal anaesthesia of shorter duration when compared to levobupivacaine and bupivacaine, and they concluded that the recovery profile of ropivacaine is useful, where early mobilization is required. eg.orthopaedic surgeries for early physiotherapy.

Koltka et al [3] compared doses of equal potency of the isobaric bupivacaine- 13 mg and ropivacaine-19.5 mg and, both with fentanyl- 20 mcg for the sub-arachnoid block in lower abdominal surgery. They found that the RF had a lower level of sensory block with a shorter duration of motor block, when compared to BF.

In a study by Lee et al [4], equal doses of intrathecal ropivacaine and bupivacaine (10 mg) with 15 mcg fentanyl were used for urology surgeries, and they reported that ropivacaine provided a similar level of sensory anaesthesia, but a shorter duration of motor block, in comparison to bupivacaine.

Chung CJ, Park JS, Yun SH, Hwang GB, Chin YJ [5] had assessed the effects of fentanyl, added with hyperbaric ropivacaine in spinal anesthesia in cesarean section. Adding fentanyl 10 micro g with hyperbaric ropivacaine 18 mg in spinal anesthesia for caesarean section improves the quality of intraoperative anesthesia and significantly increases the quality of analgesia in early postoperative period.

Graf BM [6] and his colleagues hypothesized that the differences in direct cardiovascular effects are distinguished, by the stereo selective actions of the molecules of the local anesthetic drug to specific receptors, and also by the physicochemical differences that have been triggered by the replacement of the butyl- by a propyl-residual on pipecoloxylide. They concluded that neither of the anesthetics showed inotropic effects due to stereo selective property, but the isomers of ropicavaine had lesser cardio depressant effects compared to isomers of bupivacaine because of the replacement of butyl group - by a propyl-terminal group.

Sangeeta Varun et al [7], hypothesized that intrathecal use of ropivacaine, provides a similar anaesthesia with lesser duration of motor blockade when compared to bupivacaine. In their study, they concluded that the intrathecal use of ropivacaine- fentanyl, has a faster onset, and a faster sensory regression,

delayed onset, but a comparable motor block regression, and shorter duration of analgesia when compared to intrathecal bupivacaine-fentanyl. They also concluded that ropivacaine-fentanyl when administered intrathecally, is associated with decreased episodes of hypotension, when compared to bupivacaine-fentanyl group combination.

A Yegin et al [8] had evaluated the effects of adding 25 micrograms of fentanyl intrathecally to 18 mg (6 mg/ ml) of hyperbaric ropivacaine, on the characteristics of spinal block undergoing TURP surgery, and the duration of postoperative pain relief in those patients. They concluded that adding fentanyl 25 micrograms intrathecally will improve the quality of analgesia significantly, and prolong the duration of analgesia, without causing a substantial increase in the major side-effects.

Prashanth.K.Gupta [9],and his colleagues had conducted a study which aimed at evaluating the clinical safety and efficacy of intrathecal fentanyl, used as an adjuvant to 0.75% isobaric ropivacaine on the onset, duration, intensity, and recovery time of sensory, and motor block of subarachnoid block for infra umbilical surgery. They concluded that using Intrathecal use of fentanyl, as an adjuvant to 0.75% isobaric ropivacaine had demonstrated a better clinical profile when compared to ropivacaine alone.

Singh [10] and his colleagues had studied the effect of intrathecal fentanyl on the onset, and the duration of hyperbaric bupivacaine-induced spinal block in adult male patients undergoing genitourinary or lower extremity surgeries. They concluded that adding fentanyl, 25 micrograms prolongs the duration of

bupivacaine-induced sensory blockade and also reduced the requirement of analgesia in the early postoperative period.

A Chaudhary et al [11] had conducted a study, evaluated the efficacy of intrathecal ropivacaine alone or in combination with fentanyl for transurethral resection operation, which showed that the addition of intrathecal fentanyl to ropivacaine may offer the advantage of hemodynamic stability, shorter duration of complete motor blockade, and without any increase in the frequency of major side effects.

Malinovsky JM [12] and his colleagues compared intrathecal use of ropivacaine to bupivacaine in patients scheduled for TURP .They concluded that using 15 mg of intrathecal ropivacaine provides a similar motor and hemodynamic effects, but less potent anesthesia when compared to 10 mg of bupivacaine for endoscopic urological surgery.

McNamee et al [13] studied to compare the efficacy and safety of two different concentrations of intrathecal ropivacaine, 7.5 and 10 mg/ ml, for patients undergoing total hip arthroplasty. They concluded that Intrathecal ropivacaine, in doses of 18.75 and 25 mg, was well tolerated and had provided an effective anaesthesia for total hip arthroplasty.

D. Hughes et al [14] conducted a study, aimed to reduce the incidence of motor blockade in combined spinal and epidural technique, in labour analgesia. They compared the intrathecal use of bupivacaine 2.5 mg with ropivacaine 2.5 mg, both with fentanyl 25 micrograms. They came to a conclusion that ropivacaine 2.5 mg, when used intrathecally in combination with fentanyl 25

micrograms, as part of a CSE technique had provided a safe and rapid onset of analgesia for labour, but with a lesser motor blockade when compared to a same dose of bupivacaine

Anita R Chhabra et al [15] had compared the efficacies of intrathecal adjuvants with isobaric ropivacaine for major lower limb surgeries. They compared 60 micrograms of clonidine with 25 micrograms of fentanyl, when either of them was used as adjuvant along with 15 mg of isobaric ropivacaine intrathecally, in major surgeries of the lower limb. They observed that clonidine, when used as an adjuvant intrathecally, provided a denser and longer duration of motor blockade, prolonged duration of sensory blockade, and a longer duration of post-operative analgesia when compared to fentanyl.

N Boztug et al [16] compared the effects of two different doses of intrathecal ropivacaine 8 mg and 10 mg ,with fentanyl 25 micrograms as adjuvant for out-patient arthroscopic knee surgeries. They concluded that 8 mg of intrathecal ropivacaine with 25 microgram of fentanyl provided shorter duration of sensory and motor block, compare to higher dose of 10 mg. They also concluded that small doses of ropivacaine together with fentanyl can be used safely for arthroscopic knee surgeries.

Wahedi W et al [17] in their randomised, double-blind study, administered intrathecally two different doses of ropivacaine 5mg/ml and 7.5mg/ml. A volume of 3ml was injected intrathecally to forty patients and they recorded the spinal block characteristics. They concluded that ropivacaine results in long-lasting spinal anaesthesia at concentrations of 0.5% (5mg/ml) and 0.75% (7.5 mg/ml).

Buckenmaier CC, Nielsen KC, Pietrobon R, Klein SM, Martin AH, Greengrass RA, and Steele SM [18] had compared the efficacy of ropivacaine as an alternative to lidocaine, in patients undergoing anorectal procedures as outpatient basis.

They compared intrathecal administration of hyperbaric lidocaine 25 mg with fentanyl 20 micrograms with hyperbaric ropivacaine 4 mg with fentanyl 20 micrograms. They concluded that intrathecal hyperbaric small-dose of ropivacaine with fentanyl is an acceptable anesthetic for anorectal surgeries.

Venkata HG [19] and his colleagues compared the duration of analgesia and hemodynamics using a low dose (7.5 mg) bupivacaine- fentanyl mixture with a conventional dose (10 mg) of hyperbaric bupivacaine for cesarean section. They compared between 10 mg of hyperbaric bupivacaine, and a drug combination containing 25 microgram fentanyl and 7.5 mg of hyperbaric bupivacaine, posted for elective caesarean section .They concluded that, in caesarean section, the combination of low dose bupivacaine 7.5mg and fentanyl 25 microgram is hemodynamically stable, and has a prolonged duration of analgesia when comparison to bupivacaine alone.

Bogra J et al [20] compared different doses of intrathecal bupivacaine alone and in combination with fentanyl,for caesarean section. The patient received one of the following dose i.e 8mg, 10mg, 12.5mg of bupivacaine alone, or in combination with 12.5 microgram of fentanyl. They concluded fentanyl is able to reduce the dose of bupivacaine, due to its synergistic effect on bupivacaine, and therefore reducing its harmful effects.

Van Kleef JW et al [21] aimed to determine the safety and clinical efficacy of ropivacaine, as a local anesthetic for spinal anesthesia. They studied by using either 3 mL of isobaric solution containing 0.5% (15 mg), or 0.75% (22.5 mg) ropivacaine. They concluded that subarachnoid injection of isobaric ropivacaine solutions results in a variable analgesic spread, and mostly accompanied by a good quality of motor block, in particular with the 0.75% solution.

AIM OF THE STUDY

The aim of study is to compare the efficacy and safety of intra thecal Ropivacaine- Fentanyl and Bupivacaine-Fentanyl for lower limb Orthopaedic surgeries, with respect to

1. Primary outcome- spinal block characteristics
2. Secondary outcome- haemodynamic effects and side effects.

MATERIALS AND METHODS

Study setting and design

It is a single centre, prospective, randomized, parallel group, double – blind study. This study was done in Tirunelveli medical college hospital at department of Anaesthesiology and critical care.

After obtaining institutional ethical committee approval, 60 patients between the age group of 18-60 were posted for elective lower limb orthopaedic surgeries were recruited for the study. These 60 patients were randomized using a computer generated table, into two groups of 30 patients each as follows-

Group RF - 15 mg of 0.5% Ropivacaine (3.0 ml) + 25 mcg Fentanyl (0.5 ml)

Group BF - 15 mg of 0.5% Bupivacaine (3.0 ml) + 25 mcg Fentanyl (0.5 ml)

INCLUSION CRITERIA

- ASA physical status 1 & 2
- Age 18 – 60 years
- Both gender
- Lower limb orthopaedic surgery

EXCLUSION CRITERIA

- Known hypersensitivity to any of the test drugs
- Any contra – indication to spinal anaesthesia
- Cardiac arrhythmias

PROCEDURE

Masking

Pre-filled labelled syringes loaded with the drugs were prepared by an anaesthesiologist not participating in the study. The anaesthesiologist who did the intervention and observation was unaware of the contents of the syringes and the group allocation.

When the patient arrived the operation room, IV access was established, and 500 ml of RL was started. Multipara monitor attached, and baseline parameters - EGG, NIBP, SPO2, respiratory rate were recorded. After skin infiltration with 2% lidocaine, 25GQuincke's needle was inserted through L3-4 interspace in the midline, with the patient in sitting position. Correct placement of the needle was identified by free flow of cerebrospinal fluid and 3.5 ml of the study drug was injected over 10 seconds, and the patient was then placed supine.

Standard monitoring was used throughout the surgical procedure. ECG and pulse– oximetry were continuously monitored, while NIBP was measured at 5-min intervals. Heart rate and NIBP were recorded before intrathecal injection, 3, 5, 15, 30 minutes after the intrathecal drug administration, and thereafter every 30 minutes till the end of the surgery and one hour after the end of the surgery, at the ward. Any hypotension (systolic blood pressure lower than 20% from the baseline) was treated with i.v ephedrine 6 mg and bradycardia (heart rate < 50/min) incidents was treated i.v atropine 0.6 mg increments.

PARAMETERS OBSERVED

PRIMARY

Spinal block characteristics –

Time to reach peak sensory level - Pinprick test

Time to reach peak motor block - Bromage scale grade 3

Two segment sensory regression time

Time to motor regression to Bromage scale grade 1

Duration of analgesia

Post –operative period -

Time to first analgesic demand (VAS > 4)

SECONDARY

Heart rate (< 50 /min - bradycardia)

Blood pressure (> 20 % fall from baseline SBP - hypotension)

Oxygen saturation

Pruritus

Nausea

Vomiting

Shivering

Sensory score:

Score	Response
0	normal sensation
1	loss of pin prick sensation -analgesia
2	loss of touch sensation - anesthesia

Bromage motor scale:

Grade	Response	Degree of motor block
0	No motor block	Nil (0%)
1	Unable to raise the straight leg	Partial (33%)
2	Unable to flex the knee against resistance	Almost complete (66%)
3	Unable to flex the ankle	Complete

TIME OF ONSET OF SENSORY BLOCK

The time interval between end of anesthetic injection and appearance of cutaneous analgesia in the dermatomes assessed by the pin prick test using 20 G hypodermic needle in T-12, T-10, T-8, T-6 or higher levels (T-4)

MOTOR BLOCK DURATION

It is the time taken between administration of anesthetic and the attainment of grade 0 in Bromage motor scale.

TWO SEGMENT SENSORY REGRESSION TIME

The time taken for the sensory block to regress to two segment down from the maximum level of blockade is defined as the two segment regression time

DURATION OF ANALGESIA

It is the time of administration of anesthetic and the disappearance of cutaneous level of sensation, at each dermatomal level.

POST-OP ANALGESIA DURATION

The time between the administration of anesthetic and time of analgesic requirement (visual analog scale > 4) in PACU.

Visual analog scale

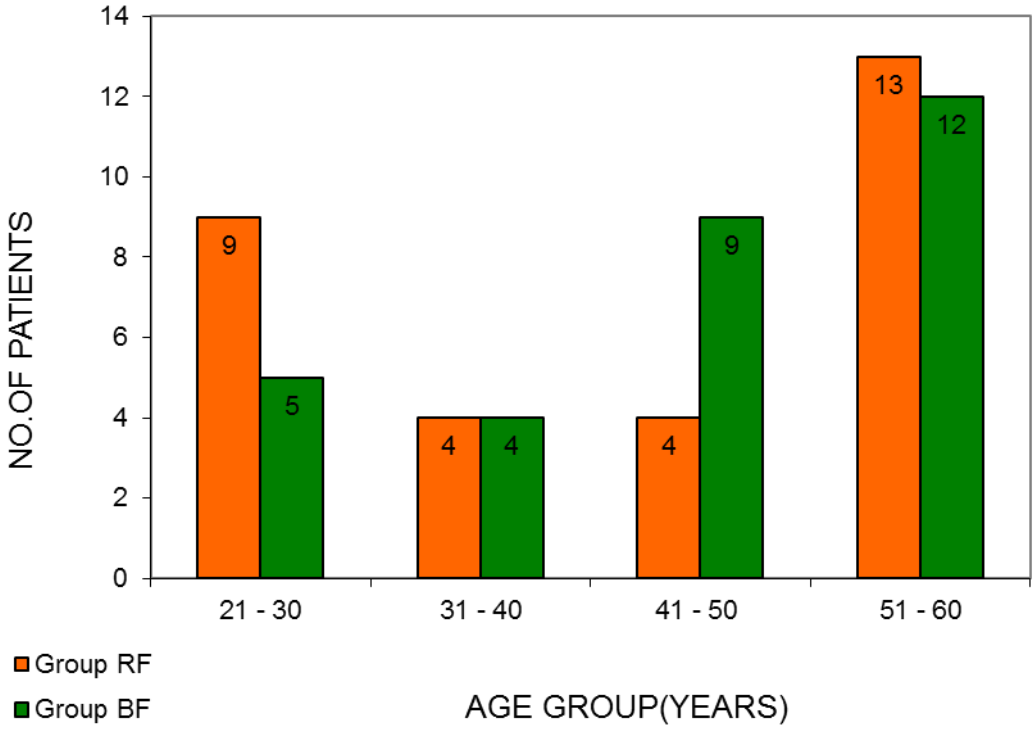
1	2	3	4	5	6	7	8	9	10

ANALYSIS AND RESULTS

Statistical Analysis:

The information which was collected regarding all the selected cases, were recorded in a master chart. Data analysis was done with the help of computer by using SPSS software and Sigma Stat 3.5 version (2012). Using this software, percentage, mean, standard deviation and ‘p’ value were calculated through one way ANOVA, and Chi square test and a P value of < 0.05 was taken as significant.

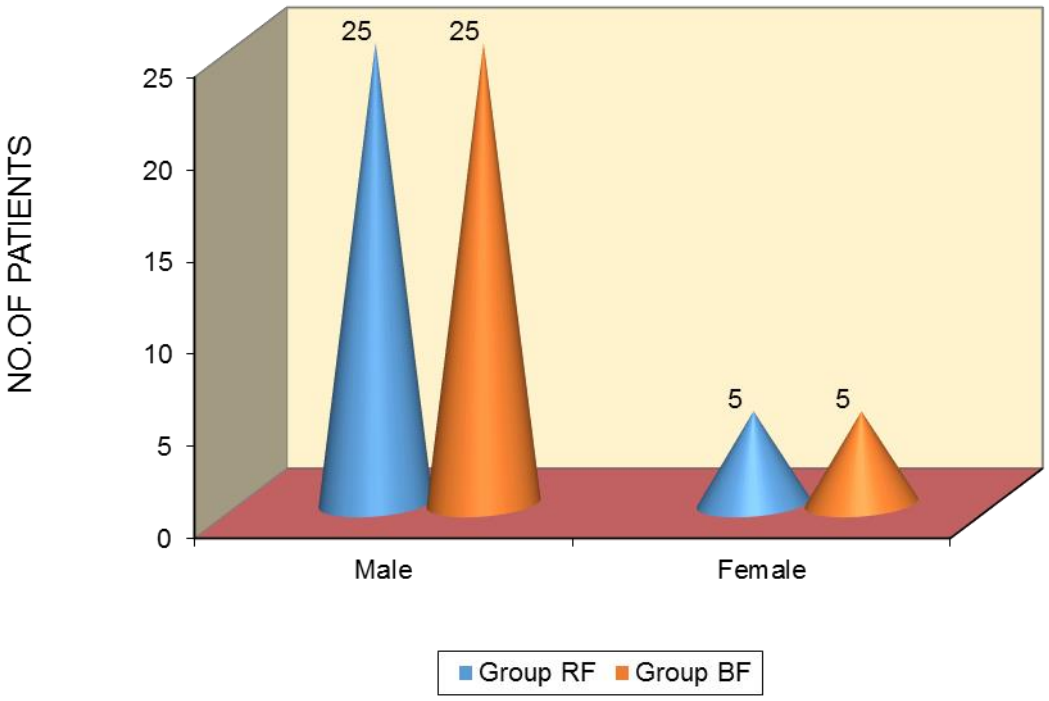
AGE DISTRIBUTION



Age in years	Group RF	Group BF
21 - 30	9	5
31 - 40	4	4
41 - 50	4	9
51 - 60	13	12
Total	30	30
Mean	42.97	44.93
SD	13.91	10.83
p value	0.544 Not significant	

The age distribution between two groups were comparable.

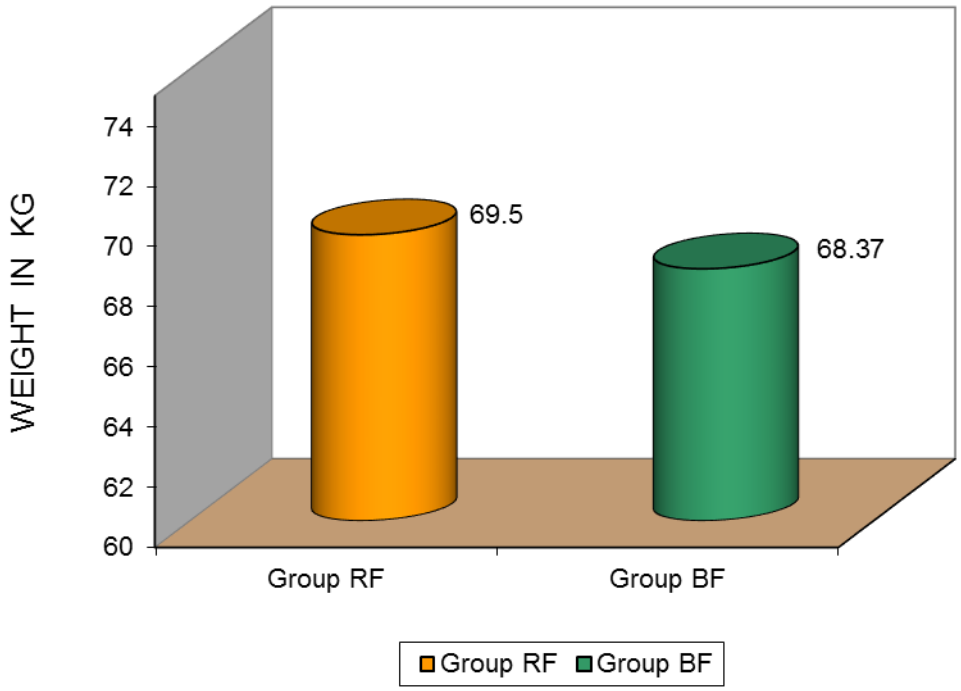
GENDER DISTRIBUTION



Gender	Group RF	Group BF
Male	25	25
Female	5	5
Total	30	30
p value	0.848 Not significant	

The distribution of gender between the two groups was comparable.ie statistically not significant.

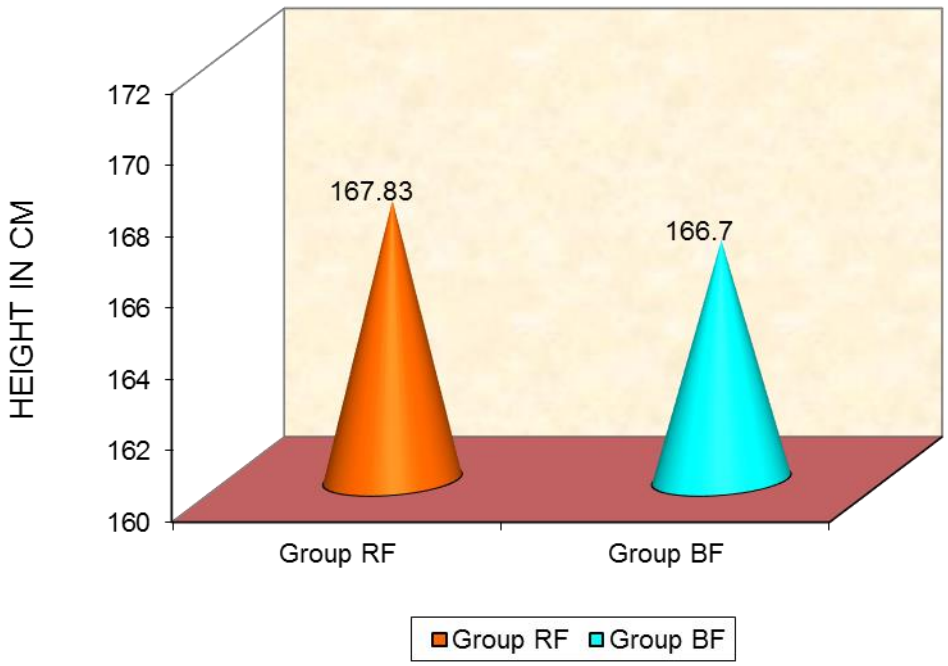
COMPARISON OF WEIGHT



Weight	Group RF	Group BF
Mean	69.5	68.37
SD	7.22	5.01
p value	0.482 Not significant	

The mean weight distribution between two groups were comparable. i.e statistically not significant.

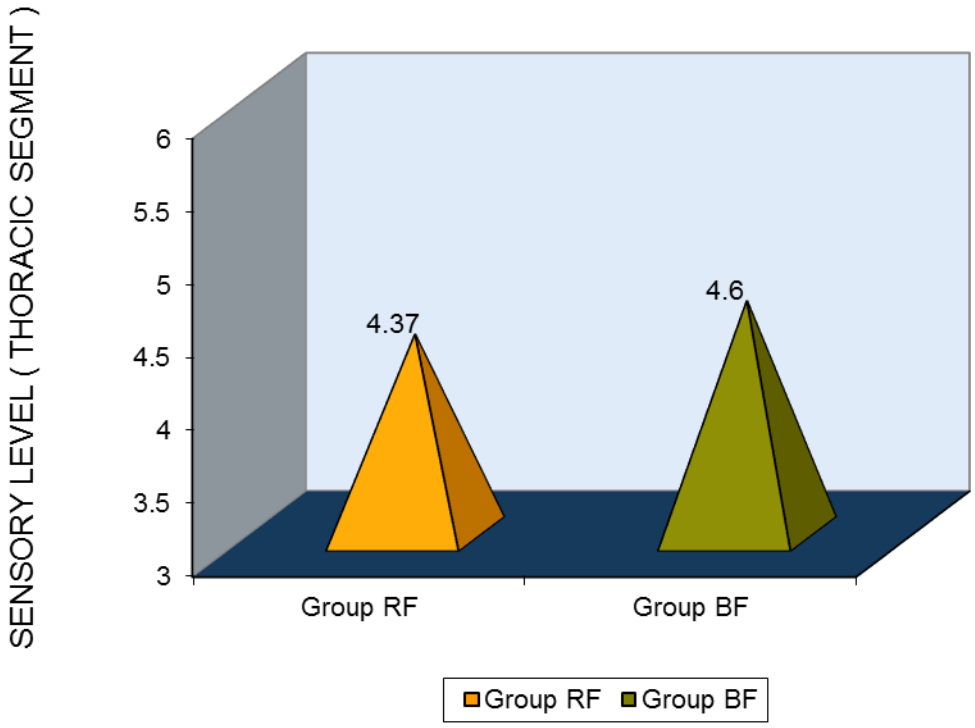
COMPARISON OF HEIGHT



Height	Group RF	Group BF
Mean	167.83	166.7
SD	8.11	7.75
p value	0.582 Not significant	

The mean distribution of height between two groups were comparable. i.e statistically not significant.

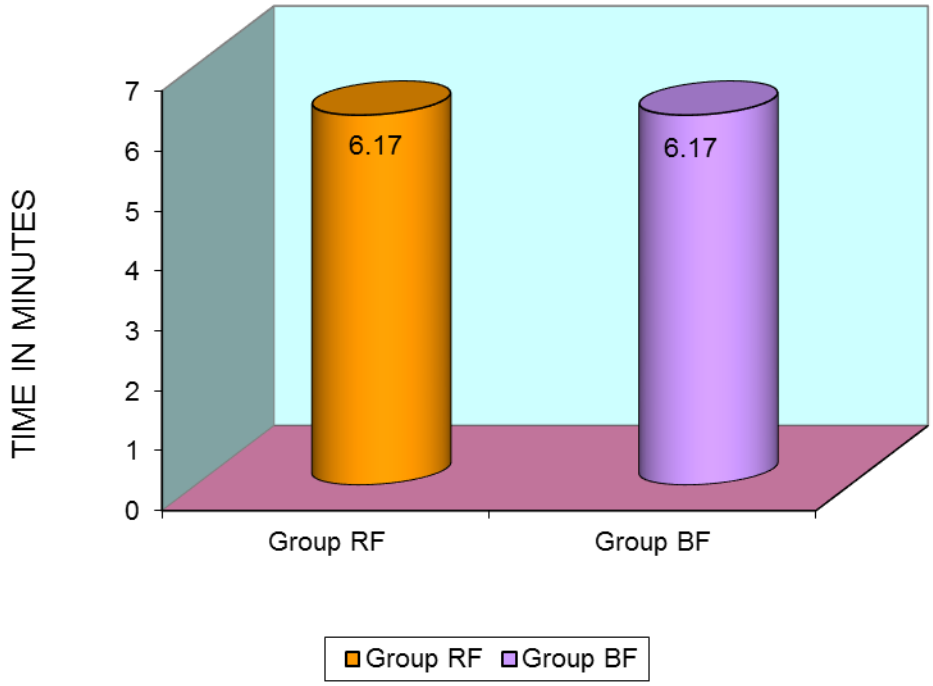
PEAK SENSORY LEVEL (THORACIC)



Peak sensory level (thoracic)	Group RF	Group BF
Mean	4.37	4.6
SD	0.85	0.77
p value	0.270 Not significant	

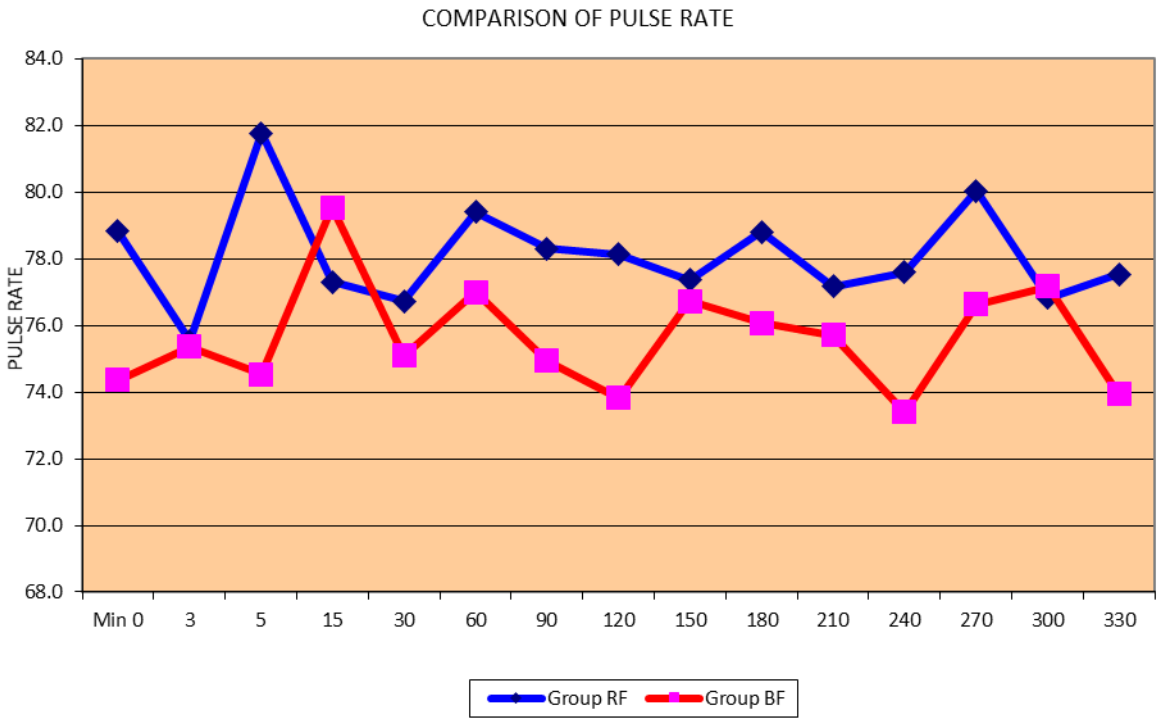
The peak sensory levels attained between the two groups were comparable. They are statistically not significant.

TIME TO REACH PEAK SENSORY LEVEL

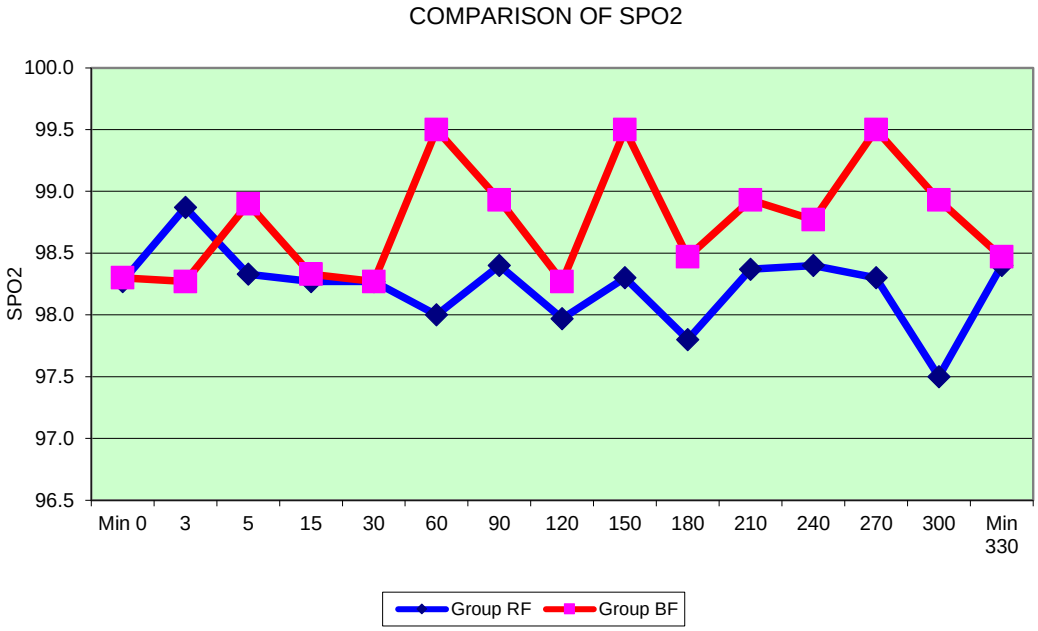


Time to reach peak sensory level in min	**Group RF**	**Group BF**
Mean	6.17	6.17
SD	0.91	0.79
p value	1.0 Not significant	

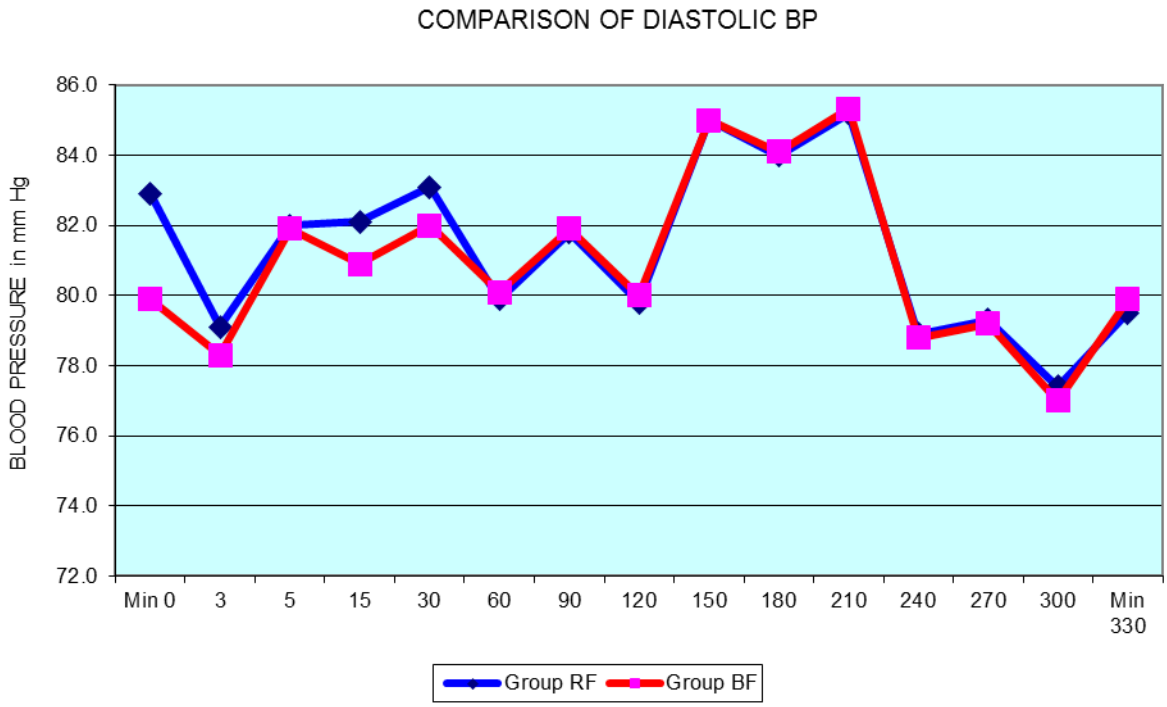
The time to reach peak sensory level between the two groups is statistically not significant.



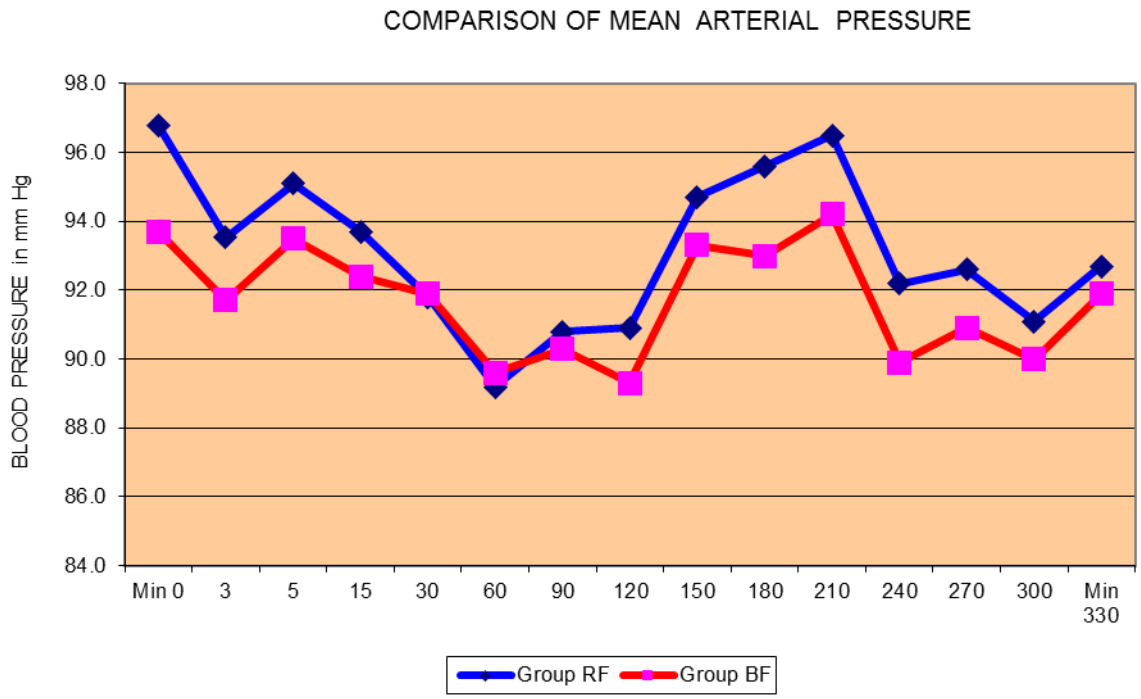
The distribution of pulse rates between the two groups were comparable. ie, statistically not significant.



The distribution of SPO2 between the two groups were comparable. ie, There is no statistical significance between the two groups in relation to SPO2.

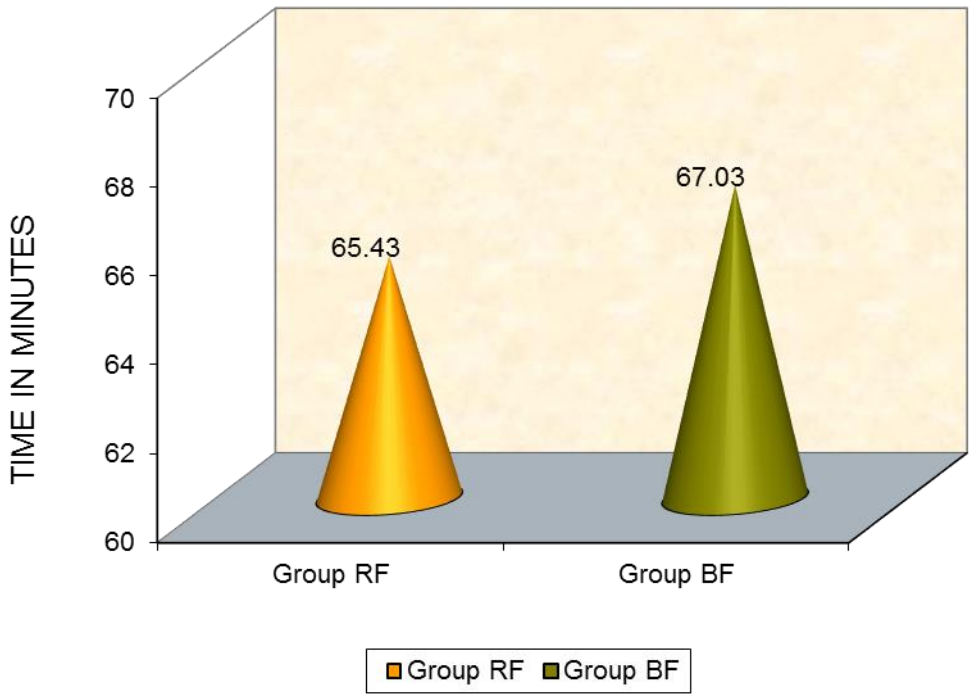


The distribution of diastolic blood pressure between the two groups were comparable .ie, there is no statistical significance between the two groups in relation to diastolic BP.



The distribution of mean arterial pressure between the two groups were comparable .ie, statistically not significant.

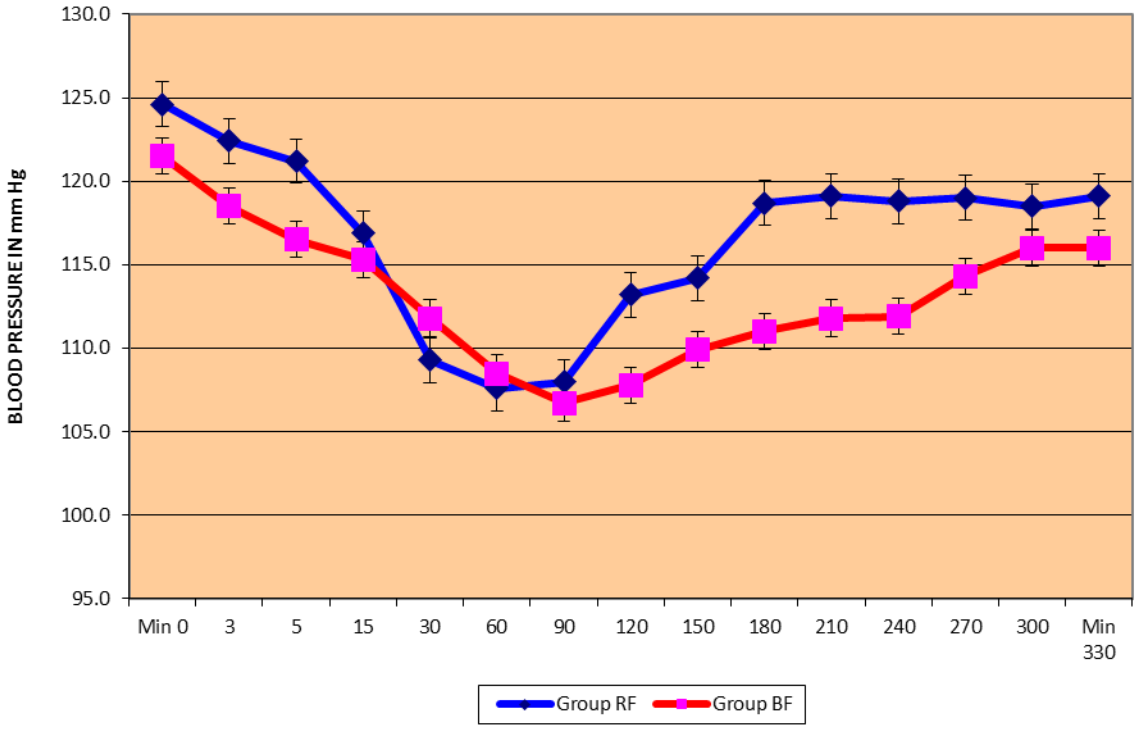
TWO SEGMENT SENSORY REGRESSION TIME



Two segment sensory Regression time	Group RF	Group BF
Mean	65.43	67.03
SD	3.12	3.71
p value	0.076 Not significant	

The two segment sensory regression time between the two groups were comparable. i.e statistically not significant.

COMPARISON OF SYSTOLIC BP



After an initial moderate fall produced by the sympathetic blockade in both groups, the systolic BP got stabilized after 90 min in RF group, indicated by the recovery of BP to a higher level comparing to BF group , This reflects the better haemodynamic stability in RF group.

There is a statistical significant difference among the two groups with respect to systolic blood pressure.

This also coincides with the early recovery of motor power in RF group, when compared to the BF group.

SYSTOLIC BLOOD PRESSURE

Systolic BP	Group RF	Group BF	SD	SD	P
Min 0	124.6	121.5	3.73	2.45	<0.001
3	122.4	118.5	4.79	4.52	0.002
5	121.2	116.5	3.52	4.31	<0.001
15	116.9	115.3	2.55	1.91	0.006
30	109.3	111.8	2.02	2.76	<0.001
60	107.6	108.5	2.88	3.98	0.333
90	108.0	106.7	2.70	3.15	0.021
120	113.2	107.8	2.24	1.06	<0.001
150	114.2	109.9	2.49	0.96	<0.001
180	118.7	111.0	1.51	1.47	<0.001
210	119.1	111.8	1.76	1.16	<0.001
240	118.8	111.9	3.24	1.88	<0.001
270	119.0	114.3	2.44	2.20	<0.001
300	118.5	116.0	2.79	1.88	<0.001
Min 330	119.1	116.0	0.83	1.68	<0.001

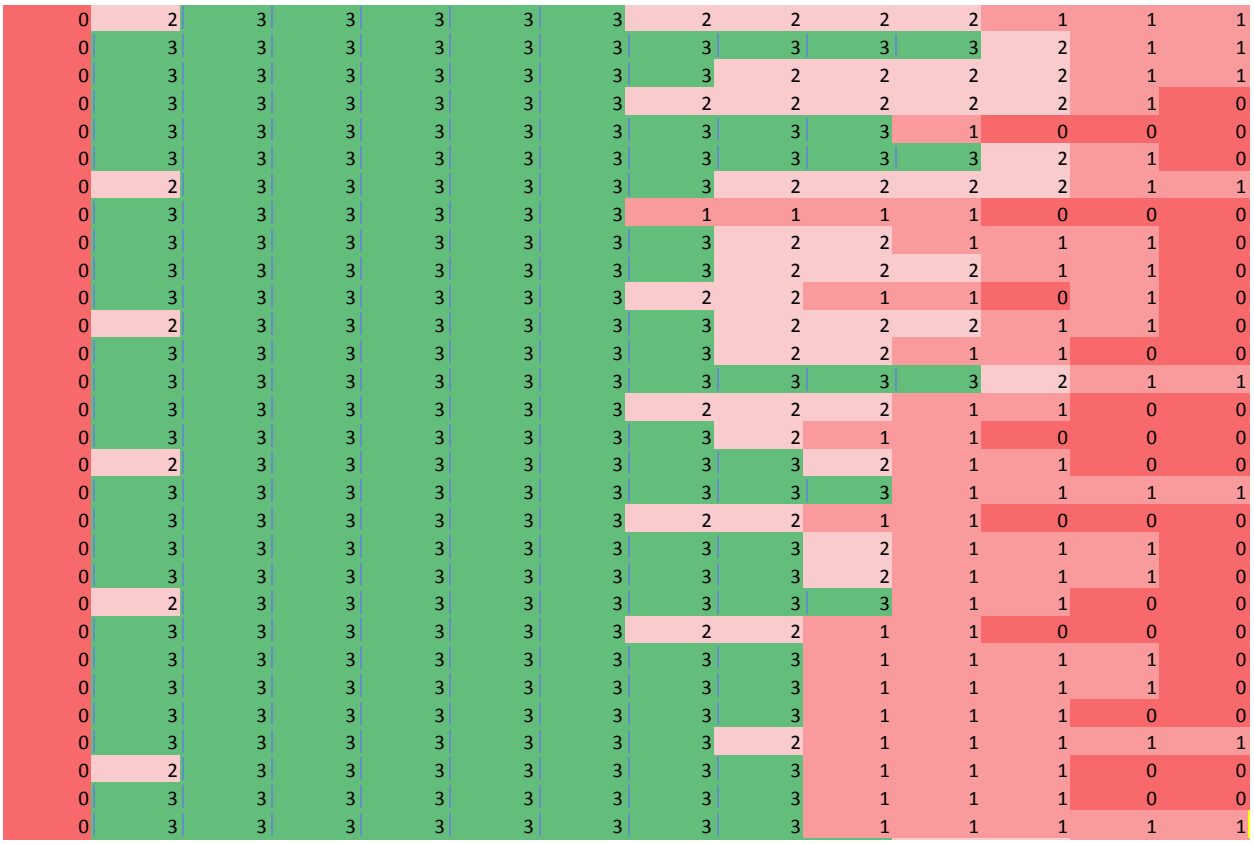
There was statistically significant difference in the systolic blood pressure between the two groups from 120 to 240 minutes. i.e $p < 0.05$. ie. There is early stabilization of systolic BP in group RF.

DURATION OF MOTOR BLOCK

Ropivacaine

Duration of motor block in minutes.

0	5	10	30	60	90	120	150	180	210	240	270	300	330



Bromage scale

There is an early recovery of motor block in ropivacaine –fentanyl group when compared to bupivacaine-fentanyl group. Most patients had full motor recovery by 300 minutes.

Bupivacaine

Duration of motor block in minutes.

0	5	10	30	60	90	120	150	180	210	240	270	300	330
0	3	3	3	3	3	3	3	3	3	2	2	1	1
0	3	3	3	3	3	3	3	3	2	2	2	1	1
0	3	3	3	3	3	3	3	3	2	2	2	1	1
0	3	3	3	3	3	3	3	3	2	1	1	1	0
0	3	3	3	3	3	3	3	3	3	2	2	2	1
0	3	3	3	3	3	3	3	3	2	2	2	1	1
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0	3	3	3	3	3	3	3	3	2	2	2	2	1
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0	3	3	3	3	3	3	3	3	2	2	1	1	0
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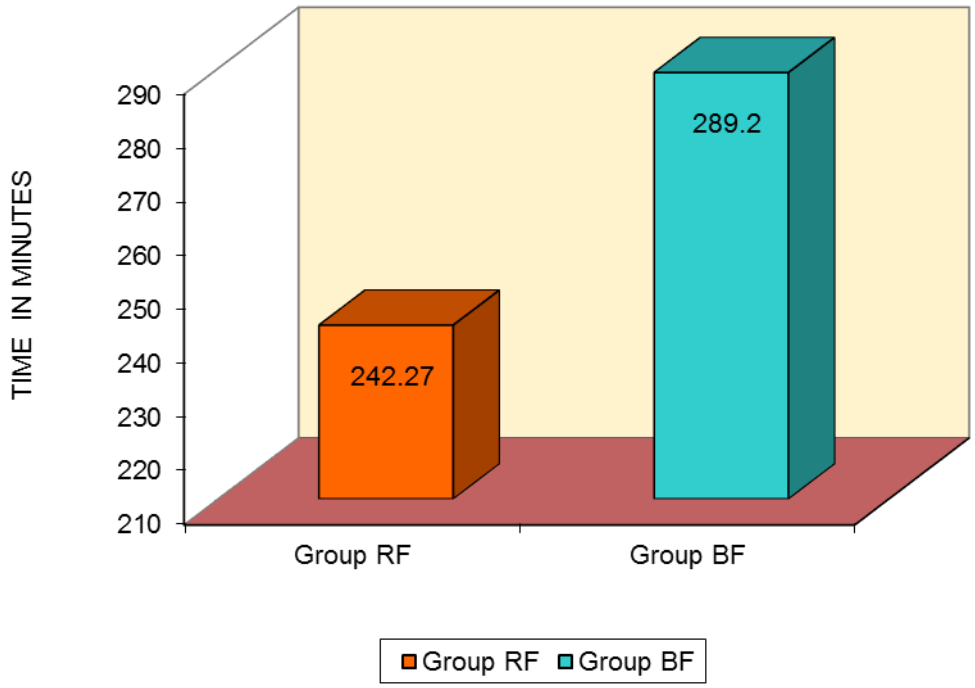
0	3	3	3	3	3	3	3	3	3	2	1	1	1
0	3	3	3	3	3	3	3	2	2	2	2	1	1
0	3	3	3	3	3	3	3	2	2	2	1	1	1
0	3	3	3	3	3	3	3	3	1	1	1	1	1

Bromage scale

The duration of motor block was prolonged in RF group as evidenced by more patients in bromage scale 3 even in 180 minutes.

DURATION OF ANALGESIA



Duration of Analgesia (min)	Group RF	Group BF
Mean	242.27	289.2
SD	12.81	16.38
p value	< 0.001 Significant	

There is a statistical significance in the difference between the two groups RF and BF. p value < 0.001 .ie, The duration of analgesia is more in BF group .

SIDE EFFECTS

PARAMETER	Group RF	Group BF
Hypotension	3	8
Bradycardia	1	1
Nausea- vomiting	1	2
Shivering	1	1
Pruritus	-	-

DISCUSSION

Ropivacaine is a long acting, enantiomerically pure (S-enantiomer) amide local anaesthetic, and with a low lipid solubility. The low lipid solubility of ropivacaine relates the lesser duration of analgesia comparing to Bupivacaine. Intrathecal ropivacaine, in animal studies has shown to produce effective sensory block, but the duration of motor block is shorter than intrathecal bupivacaine, with no signs of neurological side effects.

The early motor recovery of ropivacaine is due to the blockade of nerve fibers involved in transmission of pain (Aδ and C fibers) to a greater degree, comparing to controlling of motor functions (Aβ fibers).This feature favors its use where early ambulation is needed as in orthopaedic surgeries, for starting physiotherapy. This feature also allows for the detection of any neurological side-effects, if any, occurred.

The present study has demonstrated that using either ropivacaine or bupivacaine intrathecally, with fentanyl as an adjuvant has provided satisfactory anesthetic conditions for lower limb ortho surgeries. Most of the sub-arachnoid block characteristics were similar. There was a significant early motor recovery in RFgroup with haemodynamic stability, but BF provided a prolonged duration of post-operative analgesia.

I proposed to study the efficacy of ropivacaine for major orthopaedic surgeries as an alternative to bupivacaine, using equimilligram dose (15 mg) as used by Luck et al. While maintaining the advantage of low dose local anaesthetic intrathecally, the use of analgesic adjuvants can improve the quality of intra -operative anaesthesia. Lipid soluble opioids such as sufentanil and fentanyl are the most commonly used adjuvants. Studies have shown that intrathecal opioids can enhance greatly the duration of analgesia of sub-therapeutic doses of local anaesthetics. Fentanyl added to local anaesthetic agent intrathecally seems to be the most frequently used combination in spinal anesthesia, to enhance and increase the duration of sensory block, without intensifying the duration of motor blockade or prolonging the recovery from spinal anaesthesia.

Both intrathecal RF and BF produced an initial moderate fall in blood pressure in keeping with the expected sympathetic blockade produced by the spinal anaesthesia. Although the Systolic BP stabilized after 30 min, there was a statistically significant difference among the two groups from 120 to 240 minutes, where the systolic BP comes near the baseline values in RF group. This recovery profile of systolic blood pressure in the ropivacaine-fentanyl group more or less coincides with the recovery of motor block.

My results are consistent with Lee et al. as I observed comparable levels of highest dermatome blocked, the time taken to reach the peak sensory and

motor level and the two segment sensory regression time. The motor block was significantly shorter with Group RF, although it outlasted the duration of surgery.

This feature is desirable as it encourages early ambulation, voiding and physiotherapy. Neurological side effects, if any, can also be detected early. The mean time duration of analgesia is significantly prolonged in Group BF when compared to Group RF.

No patient in either group required intra-operative analgesia, since the duration of surgery is within the duration of sensory block in both groups.

Intra operative hypotension requiring treatment with ephedrine occurred in 3 patients in Group RF as compared to 8 patients in Group BF. One patient in each group was also treated with 0.6 mg i.v atropine for bradycardia. The most common adverse effect noted was nausea and vomiting, experienced in both the groups. Shivering also occurred in both the groups.

LIMITATIONS OF THE STUDY

Though equimilligram doses of Ropivacaine and Bupivacaine were compared, the differences in baricity were not taken into consideration. Any impact of baricity on the spinal block characteristics was not measured, as only the dose was considered.

Another limitation was the small sample size.

CONCLUSION

Intrathecal ropivacaine-fentanyl provides a satisfactory anesthesia and has a better hemodynamic stability for lower limb orthopaedic surgeries.

The shorter duration of motor block compared to intrathecal Bupivacaine – Fentanyl is helpful in terms of early ambulation, voiding and for starting physiotherapy earlier.

Although certain trends could be established in this study with encouraging results, further studies with larger sample sizes are needed to form a definitive opinion regarding the application of intrathecal Ropivacaine.

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PROFORMA

COMPARITIVE STUDY OF INTRATHECAL

ROPIVACAINE –FENTANYL AND BUPIVACAINE- FENTANYL

FOR LOWER LIMB ORTHOPAEDIC SURGERIES

NAME	AGE	DIAGNOSIS
SEX	HEIGHT	PROCEDURE
AGE	WEIGHT	ANAESTHESIOLOGIST
WARD		SURGEON
ASA GRADE		

GROUP; → RF

↓

BF →

PRE OPERATIVE CONDITION:

PR	CVS
BP	RS
Hb%	ABDOMEN
BT.CT	CNS
Blood grouping/typing	
Blood Sugar	Airway
Urea Mallampati score	
Creatinine	Spine
Serum Electrolytes	
Chest X-Ray	
ECG	
ECHO	

ANAESTHETIC PLAN - Subarachnoid block

PRE LOADING:

Drug:

Dosage:

Needle:

Position:

Level:

No of Attempts:

ASSESSMENT OF LEVEL OF BLOCK

Peak sensory level;

Time to reach peak sensory level (min);

Time to reach peak motor blockade (min);

Two segment sensory regression time (min);

Time to motor regression to bromage grade 1(min);

Duration of surgery (min);

Duration of analgesia (min);

Side effects;

POST OPERATIVE

VAS for Analgesia Assessement

MOTOR BLOCK GRADE

Bromage grade in minutes after sub arachnoid block.

0	**5**	**10**	**30**	**60**	**90**	**120**	**150**	**180**	**210**	**240**	**270**	**300**	**360**

ASSESMENT OF HAEMODYNAMIC PARAMETERS

PARAMETER	**0**	**3**	**5**	**15**	**30**	**60**	**90**	**120**	**150**	**180**	**210**	**240**	**270**	**300**	**330**
Pulse rate															
Spo2															
Systolic BP															
Diastolic BP															
Mean Arterial Pressure															

ABBREVIATIONS

RF Ropivacaine-Fentanyl

BF Bupivacaine-Fentanyl

ASA American Society of Anaesthesiologists

ECG Electro Cardio Gram

NIBP Non-Invasive Blood Pressure

SPO2 Pulse oximeter oxygen saturation

BP Blood Pressure

MAP Mean Arterial Pressure

IV IntraVenous

VAS Visual Analog Scale

RL Ringer Lactate

S.No	Name	Age (years)	Sex	Weight (kg)	Height (cm)	Diagnosis	Procedure	ASA	Group	Peak sensory level (thoracic)	Time to reach peak sensory level (min)	Time to reach peak motor block (min)	Two segment sensory regression time(min)	Time to motor regression to bromage grade 1(min)	Duration of surgery(min)	Duration of analgesia (min)	Side Effects
1	Balamurugan	28	M	76	176	Calcaneum #	ORIF	1	RF	4	6	8	68	252	158	262	
2	Sethuramalingam	57	M	65	160	Compound #tibia	IL nail	2	RF	3	6	7	62	250	200	260	Hypotension
3	Isakki ammal	60	F	55	152	OA knee	TKR	2	RF	3	7	8	71	238	210	256	
4	Arumugam	58	M	62	163	#BB leg	ORIF –IL nail	2	RF	4	7	8	64	222	190	252	
5	Muthukrishnan	29	M	76	174	SOF-IL nail	Implat exit	1	RF	5	8	10	64	228	210	248	
6	Alagukumar	34	M	84	181	#BB Leg	CRIF	1	RF	6	8	9	72	228	180	238	
7	Jebastin	54	M	74	164	Lateral tibial condyle #	ORIF -plating	2	RF	5	7	9	71	228	208	242	
8	Annalakshmi	58	F	61	154	NOF#	hemiarthroplasty	2	RF	4	6	7	68	226	194	236	
9	Annamalai	24	M	74	169	# Trochanter	DHS	1	RF	5	7	9	65	234	198	242	
10	Subbiah	58	M	68	168	#NOF	hemiarthroplasty	2	RF	4	6	9	64	236	208	258	
11	Ramesh	50	M	66	165	Old bimalleolar #-implant in situ	Implant exit	1	RF	5	5	7	62	208	210	222	
12	kalyaniammal	58	F	57	157	# trochanter	DHS fixation	2	RF	3	5	9	64	213	210	228	Hypotension
13	Pitchaiyan	51	M	62	174	# tibial condyle	ORIF with plate	2	RF	4	6	8	67	208	198	220	
14	Murugan	54	M	68	178	Supracondylar # femur	ORIF with butress plate	2	RF	5	7	9	63	223	225	256	Shivering
15	Ganesan	21	M	66	165	Patellar tendon injury with TBW	Implant exit	1	RF	4	5	9	67	218	168	230	
16	Rosiah	27	M	68	169	Tibial plateau #	ORIF with compression plate	1	RF	4	6	8	65	238	186	246	
17	Soundarrajan	27	M	74	174	# SOF	ORIF with K nail	1	RF	5	7	10	61	203	206	228	
18	Thangaraj	45	M	68	172	# BB leg	ORIF	2	RF	6	6	9	68	224	178	236	
19	Ganesamurthy	22	M	83	186	#BB leg	ORIF	1	RF	5	7	9	64	201	185	216	
20	Chinnathai	57	F	64	158	OA knee	TKR	2	RF	4	5	8	69	215	188	234	Bradycardia
21	Paradesi	51	M	72	165	# tibia	IL Nail	2	RF	4	5	7	66	248	186	262	
22	Muthuramalingam	43	M	74	172	# trochanter	DHS	2	RF	5	7	9	63	223	200	242	
23	Shanmugaiah	59	M	78	169	OA knee	TKR	2	RF	4	6	8	67	238	178	254	
24	Sheik mohamed	50	M	82	174	#NOF	hemi arthroplasty	2	RF	5	5	9	68	226	168	258	
25	Murugiah	38	M	68	168	Infected tibia nail	Implant exit	1	RF	4	7	10	61	214	138	232	
26	Padma	56	F	63	157	#BB Leg	ORIF	2	RF	3	5	8	68	220	176	244	Vomiting
27	Pandiyarajan	22	M	65	171	Posterior dislocation hip	ORIF	1	RF	4	6	9	62	218	188	244	
28	Muthu	35	M	73	174	#SOF	ORIF with IM nail	1	RF	6	5	7	65	228	198	242	
29	Devendran	36	M	71	168	Closed SOF	ORIF with K nail	1	RF	4	6	8	63	207	178	234	
30	Rajesh	27	M	68	158	# talus	ORIF wirh screw fixation	1	RF	4	6	9	61	213	146	246	Hypotension

S.No	Name	Age (years)	Sex	Weight (kg)	Height (cm)	Diagnosis	Procedure	ASA	Group	Peak sensory level (thoracic)	Time to reach peak sensory level (min)	Time to reach peak motor block (min)	Two segment sensory regression time(min)	Time to motor regression to bromage grade 1(min)	Duration of surgery(min)	Duration of analgesia (min)	Side Effects
31	Kumar	30	M	68	176	# tibial condyle	ORIF	1	BF	5	6	9	64	225	215	244	
32	Amalraj	58	M	72	170	# trochanter	DHS with PFN	2	BF	4	6	8	71	268	212	276	Nausea
33	Arulmurugan	44	M	76	168	# BB leg	ORIF	2	BF	4	7	9	67	275	185	288	Hypotension
34	Kumaraguru	37	M	68	169	Closed SOF	ORIF with K nail	1	BF	5	7	10	72	256	196	273	
35	Petchimuthu	55	M	68	171	# NOF	hemi arthroplasty	2	BF	5	6	9	69	305	205	315	Shivering
36	Ramalakshmi	42	F	63	155	Non union malleolar # ankle	Ankle arthrodesis	1	BF	4	5	8	73	285	215	303	
37	Angamuthu	54	M	64	165	Posterior dislocation hip	ORIF	1	BF	3	5	9	67	279	196	299	Hypotension
38	Prabhu	28	M	69	168	# tibia	IL Nail	1	BF	4	6	10	75	256	165	276	
39	Sivaraman	56	M	71	173	# talus	ORIF wirh screw fixation	2	BF	4	6	9	68	260	152	300	
40	Prakash	53	M	78	184	OA knee	TKR	2	BF	5	5	8	66	292	194	312	Hypotension
41	Arokiammal	35	F	65	155	# tibia	ORIF	1	BF	4	5	9	72	275	208	295	
42	Ganesh kumar	45	M	70	168	#SOF	ORIF with IM nail	2	BF	6	7	10	65	255	214	285	
43	Anjapuli	48	M	65	160	# tibia	IL Nail	2	BF	5	6	9	69	276	196	285	
44	Rajagopal	45	M	65	173	Calcaneum #	ORIF	2	BF	6	7	9	61	295	147	312	Hypotension
45	Aravind	22	M	73	169	Tibial plateau #	ORIF with compression plate	1	BF	4	6	9	62	257	178	277	
46	Thangapandi	38	M	68	173	Tibial plateau #	ORIF with compression plate	1	BF	5	8	10	68	266	214	285	Vomiting
47	Muthu	43	M	70	164	Supracondylar # femur	ORIF with butress plate	1	BF	4	7	9	64	248	185	275	
48	Arumugam	57	F	58	159	# trochanter	PFN	2	BF	4	6	8	64	292	218	305	Bradycardia
49	Chandran	53	M	65	163	# trochanter	DHS	2	BF	5	6	9	65	255	225	269	
50	Sivasankar	38	M	76	174	# tibia	IL Nail	1	BF	6	7	9	66	264	185	282	
51	Kumaresan	57	M	75	173	# NOF	hemi arthroplasty	2	BF	5	6	9	68	306	215	315	Hypotension
52	Rajarathinam	57	M	75	162	# trochanter	PFN	2	BF	4	7	10	62	295	185	312	
53	Balasubramani	52	M	65	155	Tibial plateau #	ORIF with compression plate	2	BF	4	6	9	67	285	178	298	Hypotension
54	Vasanthi	55	F	62	153	#BB leg	ORIF	2	BF	4	7	9	63	275	196	285	
55	Moorthi	28	M	64	171	Infected tibia nail	Implant exit	1	BF	5	5	8	61	260	142	276	
56	Ravikumar	57	M	76	178	Old bimalleolar #-implant in situ	Implant exit	2	BF	6	6	9	72	285	158	295	Hypotension
57	Thangaraju	43	M	65	163	Supracondylar # femur	ORIF with butress plate	2	BF	5	6	9	68	263	216	276	Hypotension
58	Veerapandi	24	M	69	168	Compound #tibia	IL Nail	1	BF	4	7	9	71	258	194	277	
59	Petchiammal	45	F	65	153	OA Knee	TKR	2	BF	4	5	8	66	275	186	297	
60	Velmurugan	49	M	63	168	#BB leg	ORIF	2	BF	5	6	8	65	276	195	289	Hypotension

S.NO	GROUP	SYSTOLIC BP (SBP) in minutes																DIASTOLIC BP (DBP) in minutes													
		0	3	5	15	30	60	90	120	150	180	210	240	270	300	330		0	3	5	15	30	60	90	120	150	180	210	240	270	300	330
1	RF	126	125	123	119	110	111	108	113	114	119	118	116	116	117	119		84	80	84	80	84	81	81	81	85	86	87	76	84	79	80
2	RF	128	126	124	118	109	106	107	115	116	117	119	118	119	116	120		85	79	83	83	85	82	80	78	86	82	84	78	83	80	81
3	RF	130	128	126	120	112	112	114	120	122	122	124	126	124	124	120		86	80	84	84	86	82	84	82	86	86	88	86	84	80	84
4	RF	118	108	114	110	100	100	106	110	110	116	116	114	116	116	118		76	78	80	80	80	78	80	78	84	82	82	72	74	74	76
5	RF	119	115	116	114	111	110	107	111	112	117	117	115	117	118	119		119	79	81	81	81	79	82	79	85	83	83	73	75	76	77
6	RF	126	125	123	119	110	111	108	113	114	119	118	116	118	116	118		80	78	82	82	83	80	83	80	86	84	88	75	78	78	79
7	RF	128	126	124	118	109	106	107	115	116	117	119	118	116	117	119		84	80	84	80	84	81	81	81	85	86	87	76	84	79	80
8	RF	125	124	123	119	108	105	108	114	118	119	116	117	119	116	120		85	79	83	83	85	82	80	78	86	82	84	78	83	80	81
9	RF	129	126	125	118	109	103	111	113	116	120	117	116	118	119	119		86	80	80	84	86	78	82	82	84	84	86	82	80	74	83
10	RF	128	127	124	119	110	104	112	111	114	119	119	118	119	117	118		81	78	84	80	82	79	81	81	85	86	85	85	81	75	77
11	RF	129	125	123	117	109	109	113	116	113	117	118	117	116	119	120		76	79	83	83	81	80	80	78	84	85	84	74	75	76	76
12	RF	122	120	119	116	110	111	112	111	116	118	119	116	119	116	119		77	80	81	84	80	81	84	79	85	82	82	75	77	75	77
13	RF	124	126	125	118	111	109	110	116	115	120	118	117	116	118	118		78	78	80	80	83	82	80	82	84	84	86	73	78	78	79
14	RF	129	124	123	119	110	108	111	112	113	121	122	120	119	117	120		79	79	84	81	84	78	83	79	86	85	84	85	79	79	80
15	RF	126	122	120	116	109	107	106	111	112	117	120	122	122	122	119		80	80	83	84	85	79	84	78	85	83	82	84	84	80	76
16	RF	120	123	122	118	108	106	109	112	115	119	122	123	121	123	118		81	79	80	83	85	81	82	82	84	85	85	83	79	78	79
17	RF	124	126	125	112	110	109	110	115	114	118	120	124	122	124	120		84	80	81	80	80	82	83	79	86	84	88	80	78	79	82
18	RF	119	111	115	111	109	111	109	116	115	117	119	125	123	123	119		86	78	82	84	86	78	80	81	84	82	84	81	77	75	84
19	RF	129	126	122	119	110	106	107	114	112	119	118	119	118	119	118		78	79	83	80	84	79	84	80	85	83	85	82	75	79	83
20	RF	123	121	120	117	109	105	107	111	113	120	119	118	117	114	120		85	80	80	83	83	82	83	79	86	86	86	73	74	80	80
21	RF	119	126	124	115	108	104	100	112	111	121	120	119	118	116	119		84	79	84	84	85	78	80	78	84	84	82	79	75	74	76
22	RF	128	127	123	116	109	108	109	111	119	118	119	118	119	119	118		77	78	80	81	80	79	82	80	85	82	88	80	84	75	78
23	RF	127	125	122	118	110	107	108	114	113	119	118	116	117	116	120		85	79	83	80	84	80	81	81	86	86	84	81	80	79	79
24	RF	123	119	117	119	111	110	111	112	111	120	119	115	116	115	119		86	80	80	83	86	81	83	82	84	84	87	73	80	78	80
25	RF	120	118	115	116	109	111	112	113	115	117	118	119	118	117	120		78	78	81	84	80	82	83	79	85	85	86	75	84	77	75
26	RF	127	121	124	119	108	107	108	116	114	118	119	117	119	120	118		80	79	83	82	83	79	83	78	86	82	87	77	82	75	79
27	RF	122	120	118	117	110	109	107	111	113	120	122	125	122	121	119		82	80	80	83	84	78	80	80	84	86	84	78	83	80	80
28	RF	126	123	122	118	109	105	109	114	115	119	120	122	123	120	120		84	79	84	81	82	79	84	82	86	84	87	86	76	77	83
29	RF	119	117	115	114	110	109	107	111	112	118	119	120	122	122	118		86	78	83	82	83	80	81	81	85	83	88	85	74	74	84
30	RF	124	122	120	119	111	110	109	113	114	121	120	119	121	119	120		76	80	80	84	80	79	80	78	84	85	82	82	80	80	76
31	BF	126	122	120	118	114	112	110	110	112	114	114	116	122	122	120		86	80	84	82	84	82	84	82	86	86	88	86	84	80	84
32	BF	118	98	96	108	98	96	98	106	108	108	110	108	112	114	114		74	76	80	80	80	76	80	78	84	82	82	72	74	74	76
33	BF	119	118	119	117	113	111	109	107	109	110	111	110	114	115	115		75	77	83	81	81	77	81	81	85	86	83	73	75	75	77
34	BF	122	120	117	116	112	110	108	109	110	111	112	111	113	114	116		76	78	82	80	83	78	83	82	84	84	84	74	76	76	78
35	BF	120	119	118	117	113	111	109	106	111	112	113	112	114	116	117		78	79	81	82	82	79	82	80	86	82	88	78	77	80	79
36	BF	119	116	115	114	111	110	108	109	109	110	111	113	115	114	116		77	80	80	80	83	82	80	78	84	86	87	79	80	79	80
37	BF	123	122	119	116	113	111	107	106	111	111	110	111	116	115	118		76	79	83	82	80	81	82	79	85	84	86	81	84	78	81
38	BF	119	116	114	113	112	110	109	108	110	109	113	112	117	116	116		79	80	82	80	83	80	84	80	86	85	82	85	82	74	76
39	BF	119	118	117	116	113	100	108	107	109	110	112	111	113	114	114		80	76	80	81	82	81	83	81	84	86	84	84	83	75	80
40	BF	125	121	119	117	110	109	107	108	111	109	110	109	112	116	119		86	78	83	82	81	80	82	82	85	83	87	78	80	76	84
41	BF	122	119	116	115	112	111	109	107	109	110	111	110	113	117	114		82	77	84	80	80	80	81	78	86	84	88	76	77	77	76
42	BF	123	120	119	116	113	110	106	109	111	113	112	111	114	119	116		81	76	80	82	83	82	80	79	84	85	82	77	78	79	84
43	BF	121	118	116	115	112	109	107	107	109	110	113	115	116	118	117		86	80	82	81	82	80	84	82	85	82	83	73	79	80	80
44	BF	120	119	115	114	113	110	109	108	110	111	110	115	113	114	115		75	77	83	80	80	81	80	78	86	86	86	75	75	79	81
45	BF	124	122	119	116	112	111	108	107	109	110	112	114	112	115	116		76	78	80	82	84	82	84	79	84	84	84	75	80	74	84
46	BF	119	117	116	115	111	108	106	109	110	113	111	112	113	116	114		77	79	84	80	80	79	83	80	85	86	87	85	81	76	79
47	BF	122	120	119	114	113	109	107	108	109	111	113	111	112	116	119		78	80	83	81	83	82	82	81	86	82	88	86	82	75	76
48	BF	120	119	116	113	112	111	109	107	110	113	112	115	116	114	117		79	77	80	80	82	80	81	82	84	83	87	73	83	74	74
49	BF	125	121	119	117	113	110	108	109	111	112	110	111	113	117	116		80	79	83	81	84	82	80	78	85	84	85	74	84	80	82
50	BF	124	120	118	116	112	100	99	108	109	110	113	112	114	116	114		83	78	82	82	80	79	84	79	86	85	84	72	78	79	84
51	BF	119	116	115	115	111	109	100	107	110	111	112	112	116	115	117		84	80	80	80	83	82	83	82	84	84	82	78	79	74	83
52	BF	123	122	119	116	113	108	109	108	109	110	111	110	114	116	114		85	76	84	81	82	81	80	81	85	82	83	80	74	75	80
53	BF	119	115	114	113	112	100	101	107	110	111	113	112	113	117	116		86	80	80	82	84	79	81	78	86	86	88	82	75	76	78
54	BF	122	120	119	117	113	111	109	109	111	113	111	113	118	119	118		84	76	83	80	80	78	82	82	85	83	87	85	76	80	80
55	BF	125	122	118	116	112	109	108	107	109	112	113	112	116	118	114		77	79	84	81	83	77	83	81	84	82	88	86	78	78	84
56	BF	124	123	116	115	111	108	107	109	110	111	112	111	113	117	116		75	80	82	82	82	80	82	78	85	84	82	84	80	79	83
57	BF	119	114	113	114	113	111	109	108	111	110	111	115	114	116	115		74	77	81	80	83	81	80	79	86	82	84	83	83	74	81
58	BF	120	119	118	116	112	109	108	109	110	113	113	112	116	114	117		86	79	80	81	80	82	84	82	84	86	87	84	84	75	82
59	BF	125	122	119	117	113	110	107	108	109	110	112	111	112	116	116		84	79	83	82	84	79	83	81	85	84	86	72	80	79	74
60	BF	119	118	117	116	113	111	109	107	111	113	113	112	113	114	114		77	80	82	81	83	81	80	78	86	85	88	75	75	80	79

S.NO	GROUP	MEAN ARTERIAL PRESSURE (MAP) in minutes															PULSE RATE in minutes													
		0	3	5	15	30	60	90	120	150	180	210	240	270	300	330	0	3	5	15	30	60	90	120	150	180	210	240	270	300	330
1	RF	98	95	97	93	93	91	90	92	95	97	97	89	95	92	93	78	65	62	64	62	64	62	69	75	83	67	65	68	69	63
2	RF	99	95	97	95	93	90	89	90	96	94	96	91	95	92	94	65	83	96	94	93	95	93	71	85	81	69	69	75	68	73
3	RF	101	96	98	96	95	92	94	95	98	98	100	99	97	95	96	62	64	62	64	62	64	62	63	61	62	65	62	63	62	61
4	RF	90	88	91	90	87	85	89	89	93	93	93	86	88	88	90	94	88	96	94	93	95	93	96	93	92	94	93	95	92	92
5	RF	119	91	93	92	91	89	90	90	94	94	94	87	89	90	91	63	65	63	65	65	65	63	65	62	63	94	63	65	64	62
6	RF	95	94	96	94	92	90	91	91	95	96	98	89	91	91	92	68	87	64	67	69	74	64	67	65	73	65	64	67	65	92
7	RF	99	95	97	93	92	89	90	92	95	96	98	90	95	92	93	70	88	77	69	72	73	65	69	75	83	67	65	68	69	63
8	RF	98	94	96	95	93	90	89	90	97	94	95	91	95	92	94	74	64	78	72	92	65	69	71	85	81	69	69	75	68	73
9	RF	100	95	95	95	94	86	92	92	95	96	96	93	93	89	95	78	67	88	92	72	85	68	73	92	71	72	68	85	70	83
10	RF	97	94	97	93	91	87	91	91	95	97	96	96	94	89	91	80	65	90	93	65	65	70	75	90	63	92	70	80	90	81
11	RF	94	94	96	94	90	90	91	91	94	96	95	88	89	90	91	86	83	96	94	77	69	90	77	62	83	93	90	81	92	71
12	RF	92	93	94	95	90	91	93	90	95	94	94	89	91	89	91	94	82	79	92	78	79	92	78	65	90	94	92	63	71	63
13	RF	93	94	95	93	92	91	90	93	94	96	97	88	91	91	92	63	79	95	79	92	89	71	79	69	70	92	71	95	79	83
14	RF	96	94	97	94	93	88	92	90	95	97	97	97	92	92	93	62	78	94	70	65	90	79	85	88	75	79	79	92	75	90
15	RF	95	94	95	95	93	88	91	89	94	94	95	97	97	94	90	77	75	90	67	69	92	75	88	89	85	70	75	76	85	70
16	RF	94	94	94	95	93	89	91	92	94	96	97	96	93	93	92	79	69	91	69	70	72	85	90	75	88	67	85	86	76	75
17	RF	97	95	96	91	90	91	92	91	95	95	99	95	93	94	95	88	76	74	84	80	65	76	92	61	91	69	76	77	73	85
18	RF	97	89	93	93	94	89	90	93	94	94	96	96	92	91	96	90	88	76	94	90	70	73	93	65	62	84	73	74	81	88
19	RF	95	95	96	93	93	88	92	91	94	95	96	94	89	92	95	92	64	89	64	89	83	81	65	93	92	94	81	82	80	91
20	RF	98	94	93	94	92	90	91	90	95	97	97	88	88	91	93	94	70	85	69	82	84	80	75	80	75	90	80	83	84	62
21	RF	96	95	97	94	93	87	87	89	93	96	95	92	89	88	90	74	65	77	89	69	94	84	85	92	77	65	84	82	85	92
22	RF	94	94	94	93	90	89	91	90	96	94	98	93	96	90	91	75	86	96	84	68	95	85	95	70	74	67	85	88	86	75
23	RF	99	94	96	93	93	89	90	92	95	97	95	93	92	91	93	76	77	62	82	66	64	86	96	82	82	69	86	90	88	77
24	RF	98	93	92	95	94	91	92	92	93	96	98	87	92	90	93	89	67	65	62	75	77	88	76	72	72	68	88	89	90	74
25	RF	92	91	92	95	90	92	93	90	95	96	97	90	95	90	90	90	69	88	72	88	87	90	86	62	69	72	90	92	92	82
26	RF	96	93	97	94	91	88	91	91	95	94	98	90	94	90	92	94	77	77	91	92	92	92	66	92	90	75	92	95	72	72
27	RF	95	93	93	94	93	88	89	90	94	97	97	94	96	94	93	93	78	94	65	72	90	93	67	85	89	70	93	92	75	69
28	RF	98	94	97	93	91	88	92	93	96	96	98	98	92	91	95	90	79	92	66	62	88	65	87	85	85	78	65	66	65	90
29	RF	97	91	94	93	92	90	90	91	94	95	98	97	90	90	95	64	83	80	69	93	79	77	70	75	81	80	77	78	69	89
30	RF	92	94	93	96	90	89	90	90	94	97	95	94	94	93	91	63	85	77	83	80	78	78	75	76	82	85	78	79	70	85
31	BF	99	94	96	94	94	92	93	91	95	95	97	96	97	94	96	61	63	64	65	63	67	63	64	67	63	63	64	65	64	62
32	BF	89	83	85	89	86	83	86	87	92	91	91	84	87	87	89	84	87	88	95	84	86	84	82	88	92	89	85	87	90	91
33	BF	90	91	95	93	92	88	90	90	93	94	92	85	88	88	90	62	64	65	75	82	68	83	65	68	64	63	64	68	65	64
34	BF	91	92	94	92	93	89	91	91	93	93	93	86	88	89	91	64	66	66	85	81	75	67	75	69	67	84	82	69	66	85
35	BF	92	92	93	94	92	90	91	89	94	92	96	89	89	92	92	83	64	68	93	64	76	80	81	70	68	82	65	70	88	64
36	BF	91	92	92	91	92	91	89	88	92	94	95	90	92	91	92	80	86	69	67	74	70	65	61	71	75	81	75	71	87	82
37	BF	92	93	95	93	91	91	90	88	94	93	94	91	95	90	93	75	85	70	93	75	81	63	71	85	76	64	81	85	75	65
38	BF	92	92	93	91	93	90	92	89	94	93	92	94	94	88	89	70	84	74	78	82	83	80	75	82	70	74	61	82	76	75
39	BF	93	90	92	93	92	87	91	90	92	94	93	93	93	88	91	74	82	78	72	80	86	83	78	80	81	75	71	80	68	81
40	BF	99	92	95	94	91	90	90	91	94	92	95	88	91	89	96	70	80	70	79	70	67	65	79	70	83	82	75	70	69	61
41	BF	95	91	95	92	91	90	90	88	94	93	96	87	89	90	89	76	81	75	89	79	69	82	69	69	86	80	78	69	75	71
42	BF	95	91	93	93	93	91	89	89	93	94	92	88	90	92	95	80	65	74	91	69	70	72	70	79	67	70	79	79	85	75
43	BF	98	93	93	92	92	90	92	90	93	91	93	87	91	93	92	79	66	88	89	80	75	75	80	85	69	79	69	85	80	78
44	BF	90	91	94	91	91	91	90	88	94	94	94	88	88	91	92	83	69	80	70	82	70	79	66	80	70	69	70	80	81	79
45	BF	92	93	93	93	93	92	92	88	92	93	93	88	91	88	95	82	67	77	76	75	79	78	70	81	75	80	80	81	85	69
46	BF	91	92	95	92	90	89	91	90	93	95	95	94	92	89	91	80	65	85	69	78	80	83	80	85	70	82	66	85	86	70
47	BF	93	93	95	92	93	91	90	90	94	92	96	94	92	89	90	61	66	84	67	79	85	65	70	72	79	75	70	72	89	80
48	BF	93	91	92	91	92	90	90	90	93	93	95	87	94	87	88	69	86	69	90	65	79	70	75	73	80	78	80	73	90	66
49	BF	95	93	95	93	94	91	89	88	94	93	93	86	94	92	93	68	65	75	80	80	86	79	75	79	85	79	70	79	64	70
50	BF	97	92	94	93	91	86	89	89	94	93	94	85	90	91	94	70	85	77	70	82	77	80	79	85	79	65	75	85	67	80
51	BF	96	92	92	92	92	91	89	90	93	93	92	89	91	88	94	74	87	88	66	83	80	72	78	83	86	80	75	83	75	70
52	BF	98	91	96	93	92	90	90	90	93	91	92	90	87	89	91	78	69	64	77	75	84	69	66	82	77	82	79	82	76	75
53	BF	97	92	91	92	93	86	88	88	94	94	96	92	88	90	91	79	75	70	87	77	69	70	69	69	65	83	78	69	71	75
54	BF	97	91	95	92	91	89	91	91	94	93	95	94	90	93	93	84	79	77	94	65	70	75	81	70	90	75	66	70	70	79
55	BF	93	93	95	93	93	88	91	90	92	92	96	95	91	91	94	80	75	79	65	69	72	78	82	75	91	77	69	75	89	78
56	BF	91	94	93	93	92	89	90	88	93	93	92	93	91	92	94	63	76	86	95	80	75	82	75	84	77	65	81	84	85	66
57	BF	89	89	92	91	93	91	90	89	94	91	93	94	93	88	92	78	74	85	69	82	79	79	64	69	78	69	82	69	84	69
58	BF	97	92	93	93	91	91	92	91	93	95	96	93	95	88	94	79	85	68	70	64	81	80	73	70	79	80	75	70	80	81
59	BF	98	93	95	94	94	89	91	90	93	93	95	85	91	91	88	63	79	62	80	65	86	82	82	75	65	82	64	75	65	82
60	BF	91	93	94	93	93	91	90	88	94	94	96	87	88	91	91	82	86	61	90	69	85	65	80	87	75	64	73	87	70	75

S.NO	GROUP	SPO2 in minutes																MOTOR BLOCK GRADE in minutes													
		0	3	5	15	30	60	90	120	150	180	210	240	270	300	330	0	5	10	30	60	90	120	150	180	210	240	270	300	360
1	RF	98	99	98	98	98	98	98	98	98	98	98	98	98	98	98	0	2	3	3	3	3	3	2	2	2	2	1	1	1
2	RF	99	98	99	99	97	97	99	96	97	99	99	97	99	96	97	0	3	3	3	3	3	3	3	3	3	3	2	1	1
3	RF	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	0	3	3	3	3	3	3	3	2	2	2	2	1	1
4	RF	97	98	97	97	97	97	97	96	97	96	97	97	97	96	97	0	3	3	3	3	3	3	2	2	2	2	2	1	0
5	RF	98	99	98	98	98	98	98	98	98	98	98	98	98	98	98	0	3	3	3	3	3	3	3	3	3	1	0	0	0
6	RF	99	98	99	99	97	97	99	96	97	99	99	97	99	96	97	0	3	3	3	3	3	3	3	3	3	3	2	1	0
7	RF	100	100	100	97	99	99	97	97	99	100	97	99	97	97	99	0	2	3	3	3	3	3	3	2	2	2	2	1	1
8	RF	97	98	99	99	100	100	98	98	97	96	98	100	98	98	100	0	3	3	3	3	3	3	1	1	1	1	0	0	0
9	RF	98	99	97	97	98	98	99	99	98	97	100	98	99	99	98	0	3	3	3	3	3	3	3	2	2	1	1	1	0
10	RF	99	98	98	98	97	97	98	96	100	98	99	97	100	96	97	0	3	3	3	3	3	3	3	2	2	2	1	1	0
11	RF	97	99	97	99	100	99	97	98	99	99	98	98	97	97	98	0	3	3	3	3	3	3	2	2	1	1	0	1	0
12	RF	98	100	99	100	98	98	99	97	98	96	99	99	98	100	99	0	2	3	3	3	3	3	3	2	2	2	1	1	0
13	RF	99	98	100	98	99	97	100	99	100	97	97	100	99	98	100	0	3	3	3	3	3	3	3	2	2	1	1	0	0
14	RF	98	99	99	97	97	99	98	100	97	98	100	98	97	99	98	0	3	3	3	3	3	3	3	3	3	3	2	1	1
15	RF	99	100	97	99	100	98	97	98	99	99	97	97	99	96	97	0	3	3	3	3	3	3	2	2	2	1	1	0	0
16	RF	97	98	98	97	99	97	99	97	98	100	98	99	98	97	99	0	3	3	3	3	3	3	3	2	1	1	0	0	0
17	RF	100	99	99	98	98	99	100	99	100	96	99	100	97	96	100	0	2	3	3	3	3	3	3	3	2	1	1	0	0
18	RF	97	100	100	97	97	97	98	96	98	97	97	98	99	97	98	0	3	3	3	3	3	3	3	3	3	1	1	1	1
19	RF	98	99	97	99	100	98	97	97	99	96	100	99	100	99	99	0	3	3	3	3	3	3	2	2	1	1	0	0	0
20	RF	99	98	98	100	99	97	99	99	97	98	99	97	99	98	97	0	3	3	3	3	3	3	3	3	2	1	1	1	0
21	RF	97	99	97	99	97	99	100	98	98	100	98	100	97	100	100	0	3	3	3	3	3	3	3	3	2	1	1	1	0
22	RF	98	98	99	98	98	98	98	99	97	96	97	98	98	98	98	0	2	3	3	3	3	3	3	3	3	1	1	0	0
23	RF	99	99	97	97	99	97	97	100	99	98	98	99	99	99	99	0	3	3	3	3	3	3	2	2	1	1	0	0	0
24	RF	97	100	98	100	97	98	99	97	100	97	99	97	98	97	97	0	3	3	3	3	3	3	3	3	1	1	1	1	1
25	RF	98	99	100	99	98	97	100	98	98	99	97	99	97	96	99	0	3	3	3	3	3	3	3	3	1	1	1	1	0
26	RF	100	98	99	97	97	99	97	99	97	96	99	98	99	97	98	0	3	3	3	3	3	3	3	3	1	1	1	0	0
27	RF	98	99	97	98	100	97	98	97	100	100	98	99	98	96	99	0	3	3	3	3	3	3	3	2	1	1	1	1	1
28	RF	97	100	98	99	99	100	99	99	98	98	97	97	97	98	97	0	2	3	3	3	3	3	3	3	1	1	1	0	0
29	RF	98	98	99	97	98	98	97	100	99	97	100	100	100	96	100	0	3	3	3	3	3	3	3	3	1	1	1	0	0
30	RF	99	99	97	98	97	97	100	98	97	96	99	99	98	97	99	0	3	3	3	3	3	3	3	3	1	1	1	1	1
31	BF	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	0	3	3	3	3	3	3	3	3	3	2	2	1	1
32	BF	98	97	98	97	97	99	98	97	99	97	98	98	99	98	97	0	3	3	3	3	3	3	3	3	2	2	2	1	1
33	BF	99	98	99	98	98	100	99	98	100	98	99	99	100	99	98	0	3	3	3	3	3	3	3	3	2	2	2	1	1
34	BF	97	97	98	99	99	99	100	97	99	99	98	98	99	98	99	0	3	3	3	3	3	3	3	3	2	1	1	1	0
35	BF	98	99	100	98	100	100	99	99	100	97	99	99	100	100	97	0	3	3	3	3	3	3	3	3	3	2	2	2	1
36	BF	100	98	99	100	97	99	98	100	99	100	100	98	99	99	100	0	3	3	3	3	3	3	3	3	2	2	2	1	1
37	BF	97	100	98	97	98	100	100	98	100	98	99	100	100	98	98	0	2	3	3	3	3	3	3	3	2	1	1	1	1
38	BF	98	98	99	98	99	99	99	97	99	99	98	99	99	99	99	0	3	3	3	3	3	3	3	3	2	2	2	2	1
39	BF	99	97	98	99	97	100	98	99	100	100	100	98	100	98	100	0	3	3	3	3	3	3	3	3	3	2	1	1	1
40	BF	97	99	100	97	98	99	100	100	99	97	99	99	99	99	97	0	3	3	3	3	3	3	3	3	2	2	2	2	1
41	BF	98	98	98	98	100	100	99	97	100	99	98	98	100	98	99	0	3	3	3	3	3	3	3	2	1	1	1	1	1
42	BF	97	97	99	99	99	99	98	98	99	100	100	99	99	99	100	0	2	3	3	3	3	3	3	3	3	2	2	1	1
43	BF	100	99	98	100	97	100	99	99	100	98	98	98	100	100	98	0	3	3	3	3	3	3	3	2	2	1	1	1	1
44	BF	98	98	100	97	98	99	98	98	99	97	99	99	99	99	97	0	2	3	3	3	3	3	3	3	2	2	2	2	1
45	BF	97	99	99	99	99	100	99	97	100	98	100	98	100	98	98	0	3	3	3	3	3	3	3	2	2	1	1	1	1
46	BF	99	97	98	98	97	99	98	99	99	100	99	100	99	100	100	0	3	3	3	3	3	3	3	3	2	2	2	2	1
47	BF	98	99	100	97	98	100	100	98	100	98	98	99	100	99	98	0	3	3	3	3	3	3	3	3	3	2	1	1	0
48	BF	97	100	99	100	97	99	98	100	99	97	99	98	99	98	97	0	3	3	3	3	3	3	3	2	1	1	1	1	1
49	BF	100	98	98	99	99	100	99	98	100	100	98	99	100	99	100	0	3	3	3	3	3	3	3	3	2	1	1	1	1
50	BF	99	97	100	97	100	99	100	99	99	97	100	98	99	100	97	0	3	3	3	3	3	3	3	2	1	1	1	1	1
51	BF	97	99	99	98	99	100	99	97	100	98	99	99	100	99	98	0	3	3	3	3	3	3	3	3	2	2	1	1	1
52	BF	98	98	98	100	97	99	98	99	99	99	98	100	99	98	99	0	3	3	3	3	3	3	3	3	2	1	1	1	1
53	BF	99	97	100	99	98	100	99	98	100	100	99	99	100	100	100	0	3	3	3	3	3	3	3	3	2	2	2	2	1
54	BF	100	99	99	97	97	99	100	97	99	97	100	98	99	99	97	0	3	3	3	3	3	3	3	3	2	2	1	1	0
55	BF	98	100	98	98	98	100	99	100	100	98	99	99	100	98	98	0	3	3	3	3	3	3	3	2	1	1	1	1	1
56	BF	97	97	99	100	99	99	98	97	99	99	98	98	99	100	99	0	3	3	3	3	3	3	3	2	1	1	1	1	1
57	BF	99	99	98	97	100	100	99	98	100	100	99	99	100	99	100	0	3	3	3	3	3	3	3	3	3	2	1	1	1
58	BF	100	98	100	98	98	99	100	99	99	98	100	100	99	98	98	0	3	3	3	3	3	3	3	2	2	2	2	1	1
59	BF	97	97	99	99	97	100	99	97	100	97	99	99	100	99	97	0	3	3	3	3	3	3	3	2	2	2	1	1	1
60	BF	98	99	99	97	98	99	98	98	99	99	98	98	99	100	99	0	3	3	3	3	3	3	3	3	1	1	1	1	1

ஆராய்ச்சி ஒப்புதல் படிவம்

கால்களில் எலும்பு முறிவு அறுவை சிகிச்சைக்காக முதுகுத் தண்டுவட நீரில் ஊசியின் மூலம் உபயோகப்படுத்தக்கூடிய இரண்டு மயக்க மருந்து கலவைகளின் விளைவுகள் பற்றி ஆய்வு

பெயர்	:
வயது	:
இனம்	:
உள்நோயாளி எண்	:
வார்டு	:
நோய்	:
அறுவைசிகிச்சை	:

விளக்கம் :

கால்களில் எலும்பு முறிவு அறுவை சிகிசைக்காக மயக்க மருந்தினை முதுகுத் தண்டுவட நீரில் ஊசி மூலம் செலுத்தி தற்காலிகமாக உணர்விழக்க செய்யும் முறையில் புபிவேகெய்ன் - பென்டனில் எனும் மருந்து கலவை பரவலாக உபயோகிக்கப்படுகின்றது. இந்த முறையில் ரோப்பிவேகெய்ன் - பென்டனில் எனும் ஆராய்ச்சிக்கான மருந்து கலவையை முதுகுத் தண்டுவட நீரில் ஊசிமுலம் செலுத்தி ஆறுவை சிகிச்சை செய்வதனால் ஏற்படும் பயன்கள், விளைவுகள், பக்க விளைவுகள் பற்றி எனக்கு நன்கு புரிகின்ற தமிழ் மொழில் தெளிவாக விளக்கி கூறப்பட்டது.

என்னுடைய அடையாளம் எந்த வகையிலும் இந்த ஆராய்ச்சி மூலம் வெளியே தெரியாது என்பதை அறிவேன். இந்த ஆராய்ச்சியில் இருந்து எந்த நேரமும் விலகலாம் என்பதையும் அதனால் எந்த பாதிப்பு எற்படாது என்பதையும் அறிவேன்

நான் யாருடைய நிர்பந்தமுமின்றி என் சொந்த விருப்பத்தின் பேரில் சுய நினைவுடன் இந்த ஆராச்சியில் பங்கு கொள்ள சம்மதிக்கிறேன்

இடம் : திருநெல்வேலி

நாள் :

கையொப்பம்